BRONCHIAL CARCINOMA

AS SEEN IN

NORTH BEDFORDSHIRE

1947 TO 1956

BY

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C O N T E N T S

Chapter I.

I N T R O D U C T I O N

Reason for undertaking study. Object of Thesis. Mortality statistics of Lung Cancer in England and Wales; interpretation of National figures. Present Investigation; material, area, incidence in area, composition of hospital series. Tables 1 - 8; Figure 1; Map .

Reason for Undertaking Study.

The incidence of lung cancer is higher in Great Britain at this time than in anyother country in which reliable information is available and the disease is therefore one of particular concern to medical and scientific workers in this country. There have been many publications in the last decade on lung cancer from the standpoints of epidemiology, aetiology, diagnosis and treatment. Those authors dealing with the clinical aspects of the disease have drawn their material largely from specialised

centres such as thoracic surgical or radiotherapy departments or from specialised chest hospitals. For example the Brompton Hospital by the reputation of its staff draws patients from all over this country and from abroad. Statistics from such centres have no value in assessing the problem from the point of view of natural incidence and information on this aspect has been mainly obtained from mortality statistics provided by a regional Cancer Registration scheme or by the Registrar-General's reports. It was felt therefore that the incidence and results of treatment of lung cancer could profitably be studied in a geographical area where the diagnostic services were carried out through a single general hospital. Bedford General Hospital largely fulfilled this qualification.

Object of Thesis.

It was planned to study the incidence of lung cancer in that area of the county served by the Bedford General Hospital and Chest Clinic in two ways. First from the mortality statistics of the area, available from 1950 to 1956, and second from the case records of all cases of lung cancer referred to the hospital and chest clinic from 1947 to 1956. The various clinical features and the results of treatment in those patients so referred were also analysed.

Mortality Statistics of Lung Cancer in England and Wales.

Although this work is a survey of lung cancer cases seen

in an area over a ten year period, consideration of the incidence of this condition in England and Wales as a whole will give a background to the subject.

From the Third Part (Commentary) of The Registrar General's Statistical Review of England and Wales for the year 1954, the following figures are taken.

TABLE 1.

Standardised Cancer Mortality Rates per million living

	Lung, bronchus and pleura.		All sites less lung and bronchus.	
	Males.	Females.	Males.	Females.
1901-10.	10.2	7.0	774	935
1911-20.	12.7	7.0	884	952
1921-30.	25.1	9.6	975	970
1931-39.	85.6	22.1	968	940
1940-49.	186.8	33.9	887	858
1950-54.	335.6	47.3	840	808

TABLE 2.

Crude Cancer Mortality Rates of Lung and Bronchus per million living (1954).

	Males.	Females.
England and Wales	657	102
Conurbations	808	126
Areas outside conurbations :-		
Urban areas with populations of 100,000 and over	721	94
Urban areas with populations of 50,000 and under 100,000	601	98
Urban areas with populations of under 50,000	571	82
Rural districts	453	81

Thus, lung cancer has increased by 3,190% in males and 576% in females between 1901-10 and 1950-54 while other cancers have increased by 8% in males and decreased by 13% in females. The main increase in rates commenced, in males, after the second decade of the century and in females it started a decade later. In tables showing the death rates for the three five year periods between 1940 and 1954, it is seen that below the age of 55, the rate of increase in male cancer is slackening though over the age of 55 it shows little change. The mortality rates decrease as the degree of urbanisation diminishes, a trend more obvious in males but present to a lesser extent in females.

Furthermore, other information from the same source shows that cancer of the lung and bronchus in 1950-54 constituted 27.5% of all cancer deaths in males and 5.3% in females. No other single site has now a higher cancer incidence in men, though cancer of the digestive tract as a whole has a slightly higher incidence.

Although inaccuracies in diagnosis and certification are inherent in a comparison of national mortality rates, these are least when the ratio of lung cancer death rates to total cancer rates is taken as the basis for comparison. When this is done, it is evident that the incidence of lung cancer is greater in Great Britain than any other country where reliable statistics are published with Finland running a close second and Norway having the lowest incidence of all the European countries.

Interpretation of National Figures.

Arguments have been brought forward to show that the increase is not due to a rising incidence but is due to various fallacies. Broadly, the reasons for believing the increase is not real are as follows :-

1. The increase in average length of life. Age - specific death rates correct for this and the increase is still apparent. Also the high rates for Great Britain, Finland and Switzerland and low rates for Norway and Iceland do not correspond to those countries having the highest and lowest proportion of old persons in their respective populations.

2. Improvement in diagnosis. Between 1900 and 1950 the ante-mortem diagnosis of lung cancer improved. Steiner (1953) has shown how new diagnostic methods have developed since 1910 starting with biopsies of distant metastases and continuing through the use of radiographs, bronchoscopy, resectional surgery, exfoliative cytology and diagnostic thoracotomy. Post-mortem diagnostic ability is unlikely to have changed much and there has been an increase in the incidence in autopsy series over this period (Dorn, 1953). Autopsy series from 1920 onwards have shown an increase in the proportion of lung cancers in St. Mary's and St. Bartholemew's hospitals and the Glasgow Western Infirmary (Daff, Doll and Kennaway, 1951). That physicians are more aware of the condition today due to increased publicity is undoubtedly a fact, but the increase started before the interest became widespread and was not

entirely the result.

3. Improvements in the treatment of pulmonary disease affecting young and middle aged persons, such as pneumonia, have resulted in more people living to the age when lung cancer is prevalent. Stocks (1953) has calculated that this factor could only account for 1/5 of the increase of lung cancer between 1940 and 1950. Also the argument that better treatment of pneumonia and tuberculosis lead to true certification of deaths as lung cancer that had been previously attributed to the former illnesses is invalidated by the fact that the increase was apparent long before pneumonia and tuberculosis mortality rates were substantially altered. Also the drop in these rates has been roughly equal in men and women.

4. Increased accuracy of death certification. For certificates issued after post-mortem examination accuracy is not likely to have altered greatly over half a century. Those issued on clinical grounds might however be much more accurate today. Smithers (1953) quoted several authors' figures of inaccurate ante-mortem diagnoses in patients with lung cancer. These were Kennaway and Kennaway (1947a) 42%, Clemmesen and Busk (1947) 37%, McConnell, Clarke and Downton (1952) 24% and in Smithers' own clinic 8.6%. Green (1926) and Rigdon and Kirchoff (1952) have shown that lung cancer rates in the United States varied directly with the number of doctors in the area, and by the latter authors with the number of hospital beds in the area. This, however, might have been simply the effect of the

preponderance of cases in urban areas and not the cause of it. McKenzie (1956) studied a random sample of cases certified as dying from lung cancer in England and Wales in January 1955 and found the standard of diagnosis high. In only 3% had no confirmatory procedure been adopted while in 50% of all cases and in 67% of those under 65 years, the diagnosis had been confirmed by a technique which permitted a minimum of error. He concluded that the condition was not being over-reported. It was impossible to say, of course, whether it was being under-reported then or in the past.

The main arguments put forward to support the claim that the increase is a real one are as follows :-

1. The increase has been noted all over the world even after attention was drawn to the importance of the disease in countries with well developed medical services and has been, on the whole, most obvious in highly industrialised and populous countries. The increased proportion of cases parallel with increasing urbanisation has also been noticed in these countries. This, however, may also parallel the larger number of well equipped hospitals in the larger towns, but the urban/rural ratio is not very marked among women whereas it is considerable among men. Doll (1953) stated that the difference was not due to better diagnostic facilities in towns.

2. The condition is now so common that, had the increase been spurious, it would be necessary to postulate that 50 years ago, 95% of the fatal cases were wrongly certified.

3. The differing rates of increase between the sexes is difficult

to explain other than by accepting a real increase, more in men than in women. Better diagnosis and certification, if occurring, should affect both sexes more or less equally and does not explain why the rise in the female rate started later than the male. Even if all lung cancer in women and an equivalent fraction in men had been due to better diagnosis, it would still leave an eighteen-fold increase between 1914 and 1950 to be accounted for (Dorn, 1953). The rates of increase in different age groups have been unequal. It is difficult to explain this on the grounds of improved diagnosis. In Britain the age distribution is also different from that of all other major types of male cancer and has been changing in form while its incidence has been increasing. The same phenomenon has been observed in Denmark (Clemmesen, Nielson and Jensen, 1953).

4. The mortality among Doctors, who are as well investigated as any section of the community, has been practically the same as that for the whole population (Kennaway and Kennaway, 1947b).

5. Mistaken diagnosis of tuberculosis and pneumonia: during 1930-1948 in the older age groups the death rate for tuberculosis did not fall greatly whereas that for lung cancer was increasing. If this increase was due to a change in habit of diagnosing cancer as tuberculosis one would have expected a more marked reduction in the tuberculosis death rate for that age group. Also, the rate for lung cancer shows no seasonal drop whereas death rates for pneumonia and other respiratory diseases drop markedly in the summer.

In conclusion, it may be stated that several workers who considered the increase to be spurious have subsequently modified their views (Steiner, Butt and Edmondson, 1950; Clemmesen et al, 1953), and it is now the general consensus of opinion that not only has there been a real increase in the incidence of this condition but that the increase has been considerable and alarming.

Present Investigation.

Material.

The material of the survey is drawn from two sources. (One) The population and mortality rates for the area and its administrative urban and rural districts have been obtained from the Annual Reports of the Medical Officer of Health for Bedfordshire County Council. These figures cover only 1950-1956 as previous to 1950, deaths from lung cancer were not separately recorded. Crude Mortality Rates for England and Wales have been obtained from the Registrar General's Annual Reports. (Two) Details of all traceable cases of lung cancer domiciled in the survey area who have attended the Bedford General Hospital and associated Chest Clinic between 1947 and 1956 have been reviewed. These include both out-patients and in-patients. Histological reports on any of these patients who underwent diagnostic or therapeutic procedures in hospitals outside the area have been obtained where possible although success has not always been achieved. The date of death of any patient

dying at home has been obtained from the general practitioner concerned and this co-operation has enabled the case record of every hospital patient to be completed. The follow-up of patients still alive has been taken to November, 1957.

Area.

The area covered by this survey is the northern portion of the county of Bedfordshire, this being the district served by the Bedford general hospital and chest clinic. The area consists of the contiguous municipal borough of Bedford and urban district of Kempston surrounded by an agricultural area containing three other urban districts. These latter districts are so small (populations 3,060, 7,650 and 3,870 in 1955) that I have considered them as "rural" for the purposes of this survey. Bedford and Kempston with a population of approximately 65,000 constitutes the only truly "urban" district in the area. My terms "urban" and "rural", therefore, do not correspond to the local administrative districts of these titles. The population of the rural area is approximately 98,000.

Incidence of Lung Cancer in the Area.

It is apparent that the number of cases dying each year in the area, as recorded by death certification, is greater than the number of cases referred to the hospital during that year. No correlation of patients can be obtained each year as those dying include patients seen at the hospital during several of

the previous years. However the survival of the majority of lung cancer patients is, unfortunately, so short that over a period of seven years most of the patients seen at the hospital will also be recorded in the area mortality figures. Thus from 1950-1956, 347 patients were certified as dying from this cause while 256 were seen at or treated in the hospital (74%), a loss of 91 patients an average of 13 patients each year. To obtain a complete survey of the disease in the area the accuracy of diagnosis in these thirteen patients annually and their treatment and survival should have been obtained. This has not been possible. The diagnosis in these cases has apparently been made at various centres. Some have been sent from outlying districts to hospitals in other counties which are nearer or easier of access by public transport, others have been sent to London hospitals which are a comparatively short journey away, others have been treated as private patients, usually in London, while a number have been diagnosed by the practitioner, perhaps with a domiciliary visit from a hospital consultant, but who by choice or severity of illness have not been admitted to hospital.

Table 3 shows the crude Lung Cancer Death Rates for the area and it can be seen that the population and rates vary but not synchronously. The drop in total population from 1952-1954 occurred in the rural area. There is a considerable number of service personnel, mainly in the rural districts and the number fluctuates considerably. At the 1951 census there were about 6,400 such persons in the whole county, mainly in the rural part of this survey area and about 300 in the urban area. As these

persons add to the population but any lung cancers occurring among them are not included in the returns for the area, their presence tends to lower the true incidence in the area but only by two or three per cent. The crude Mortality Rate over the years is shown graphically in Figure 1 which shows an uneven rise from 1950 to 1956.

Table 4 sets out an estimation of the number of cases to be expected in this area each year if the local incidence were the same as that pertaining to England and Wales as a whole, compared with the number actually recorded. It is seen that rather fewer deaths than expected are in fact recorded. This is partially accounted for by the fact that, as no area comparability factor for lung cancer deaths for this particular population can be obtained, no adjustment for age or sex can be applied. The rates would, however, be little altered by employing such a factor if obtainable and the difference is obviously due to the area being almost entirely rural. The incidence in this area is therefore in accord with the overall pattern in the country. The increase in death rates for lung cancer in England and Wales from 1950 to 1956 was 45% (280 - 407 deaths per million living) and in this area the increase was 41% (268 - 377 deaths per million living). Thus the rate of increase here is in accord with the national trend.

The urban/rural ratio of mortality rates is shown and varies annually from 1.5/1 to 0.6/1, an average over seven years of 1.1/1. This is rather lower than the national ratio

for towns of between 50,000 and 100,000 population and rural districts. It probably indicates that the "factor" of urbanisation does not act strongly in Bedford and Kempston.

Composition of the Hospital Series.

Table 5 sets out the number of patients with lung cancer who attended the Bedford General Hospital and Chest Clinic from 1947 to 1956 inclusive, 291 in number, analysed by year, sex and age. The departments attended, methods of diagnosis, treatment and survival will be described later. It can be seen that the numbers seen each year rose until 1952 since when they have increased little. The male/female ratio is 7.3/1 which is in accord with other published series, some of which are shown in Table 6.

The proportion of histologically confirmed cases each year is shown in Table 7. This is discussed in more detail later.

The distribution of cases throughout the area is shown diagramatically on the map. Outside Bedford and Kempston, the only marked concentration of cases occur in the urban districts of Biggleswade and Sandy towards the east of the County. The urban/rural morbidity ratio of patients in the hospital series is 1.3/1, rather higher than the ratio derived from the mortality statistics (1.1/1), showing that the diagnostic services have been employed more by the urban than the rural patients. There are equal numbers of patients below and above

the age of 60 years but the urban/rural distribution of them is different as shown in Table 8. About two-fifths of the urban cases were under 60 years of age compared with three-fifths of the rural cases. This is not due to difference in the age distribution of the population for at the 1951 census of the area the urban and rural populations (by Registrar General's definition) contained 88.2% and 88.5% of persons under 65 years of age respectively.

It must be noted that the division into an urban or rural case has depended on the patient's address at the time he or she was seen at a clinic or admitted to hospital. Unless this has been stated by the patient to be a temporary address, no effort has been made to establish where the patient has lived for the majority of his or her life. Some errors must occur, therefore, in the division into urban and rural patients but any errors might well cancel each other out.

Further analysis of the series is given in subsequent sections dealing with Case Finding, Clinical and Radiological Features in Diagnosis, Additional Diagnostic Procedures, Methods of Treatment and Prognosis. These are preceeded by two sections giving a general survey of the Aetiology and the Pathology of lung cancer with reference to the present series where applicable.

TABLE 3.

NUMBER OF DEATHS AND CRUDE DEATH RATE FOR MALIGNANT NEOPLASMS OF LUNG AND BRONCHUS.
URBAN AND RURAL DIVISIONS SURVEY AREA 1950 - 1956.

	Population			Lung Cancer Deaths			Lung Cancer Death Rates/Mill			
Year	Urban	Rural	Total	Urban	Rural	Total	Urban	Rural	Total	Urban/ Rural Ratio
1950	62,998	93,670	156,668	21	21	42	333	224	268	1.5/1
1951	63,256	100,531	163,787	20	30	50	316	298	305	1.1/1
1952	63,630	99,675	163,305	22	29	51	346	291	312	1.2/1
1953	64,110	98,670	162,780	19	23	42	296	233	258	1.3/1
1954	64,010	96,680	160,690	14	32	46	219	331	286	0.6/1
1955	64,930	96,790	161,720	22	32	54	339	331	334	1.0/1
1956	65,850	98,600	164,450	28	34	62	425	345	377	1.2/1
Prop-ortion	39.6%	60.4%	100%	42.1%	57.9%	100%			Average	1.1/1

FIGURE 1.

CRUDE DEATH RATE FOR MALIGNANT NEOPLASMS OF LUNG AND BRONCHUS. URBAN AND RURAL DIVISIONS AND TOTAL. SURVEY AREA 1950 - 1956.

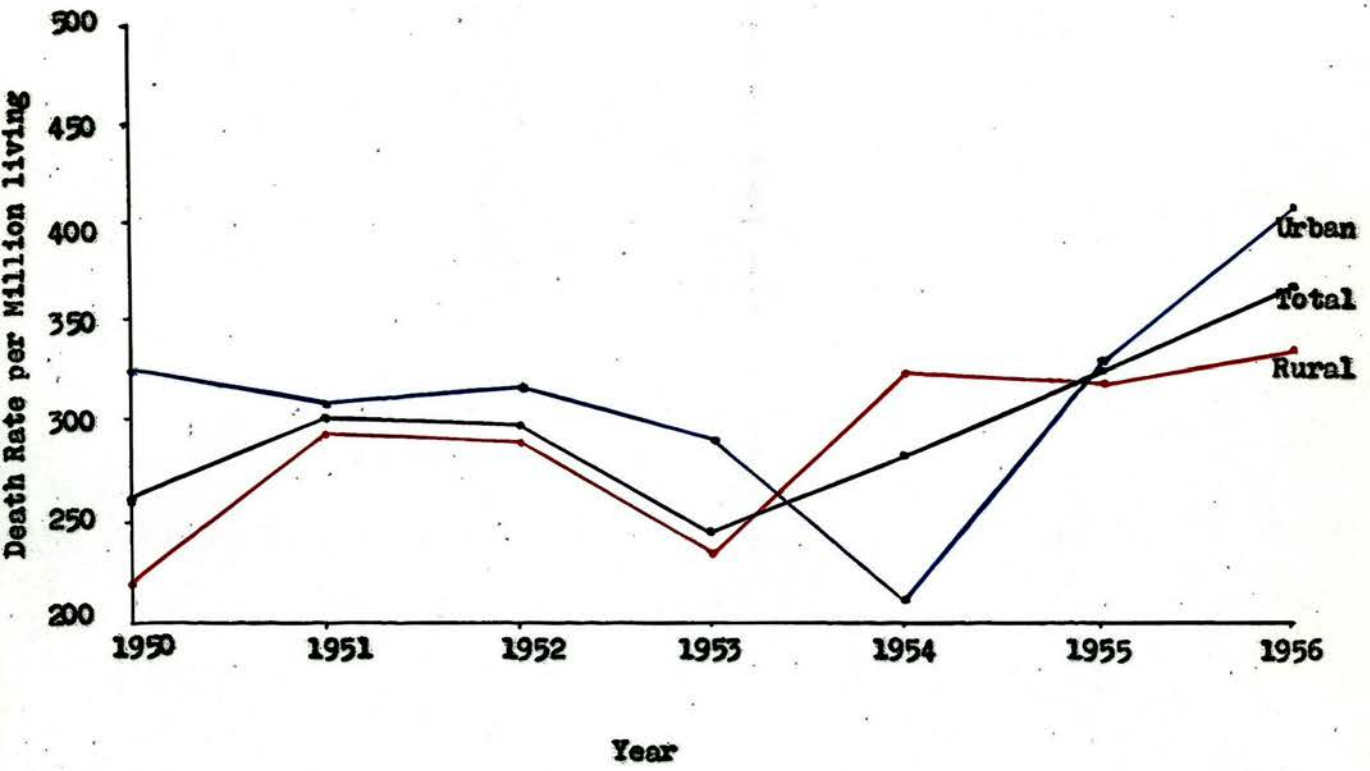


TABLE 4.

EXPECTED AND ACTUAL NUMBERS OF CASES IN SURVEY AREA AND NUMBERS SEEN IN BEDFORD GENERAL HOSPITAL 1950 - 1956.

Year	Lung Cancer Death Rate/ Million England and Wales	Expected number of cases Survey Area	Actual number of cases Survey Area	Number of cases seen Bedford General Hospital
1950	280	44	42	32
1951	303	50	50	29
1952	323	53	51	39
1953	343	56	42	34
1954	369	60	46	37
1955	388	63	54	42
1956	407	67	62	43
Total			347	256

TABLE 5.

BEDFORD HOSPITAL SERIES BY YEAR, SEX AND AGE.

Year	Sex	5-year Age Groups											Total	Total M & F
		<35	-39	-44	-49	-54	-59	-64	-69	-74	-79	- 84		
1947	M			1	1								2	2
	F												-	
1948	M			1		3	4	2	1				11	13
	F		1		1								2	
1949	M	1	1		1	1	3	7	3	1			18	20
	F			1			1						2	
1950	M				3	11	4	6	4	1			29	32
	F			1				1		1			3	
1951	M	1	1	1	2	3	6	6	3	3	2	1	29	29
	F												-	
1952	M			1	4	3	12	4	2	5	5		36	39
	F						1	1	1				3	
1953	M				1	8	10	3	1	6		2	31	34
	F						1	1	1				3	
1954	M	2	2	1	1	4	3	4	9	2	1		29	37
	F		1	1		1	2	1			1	1	8	
1955	M	1			2	3	6	8	7	5	2	1	35	42
	F	1		1		1		2	2				7	
1956	M	1		1	2	4	5	10	3	4	4	2	36	43
	F				2	2				1	2		7	
Total	M	6	4	6	17	40	53	50	33	27	14	6	256	
	F	1	2	4	3	4	5	6	4	2	3	1	35	
Total Both Sexes.		7	6	10	20	44	58	56	37	29	17	7		291

TABLE 6.

SEX RATIO IN SOME PUBLISHED LUNG CANCER SERIES.

Author	Sex Ratio M/F
Miyaji, Kitamura, Senoo, Oda and Murata (1955)	5/1
Aufses (1953)	5.2/1
Taylor and Waterhouse (1950)	6/1
Boyd, Smedal, Kirtland, Kelley and Trump (1954)	6.6/1
Jones, Robinson and Meyer (1955)	6.8/1
Ochsner, DeCamp, DeBakey and Rae (1952)	7.7/1
Gibbon, Allbritten, Templeton and Nealton (1953)	10/1
Brooks, Davidson, Thomas, Robson and Smithers (1951)	10.7/1
Toft (1955)	11.3/1
Nicholson, Fox and Bryce (1957)	13.1
Ehler, Strannahan and Olson (1954)	13.3/1

TABLE 7.

EXTENT OF HISTOLOGICAL CONFIRMATION IN HOSPITAL SERIES.

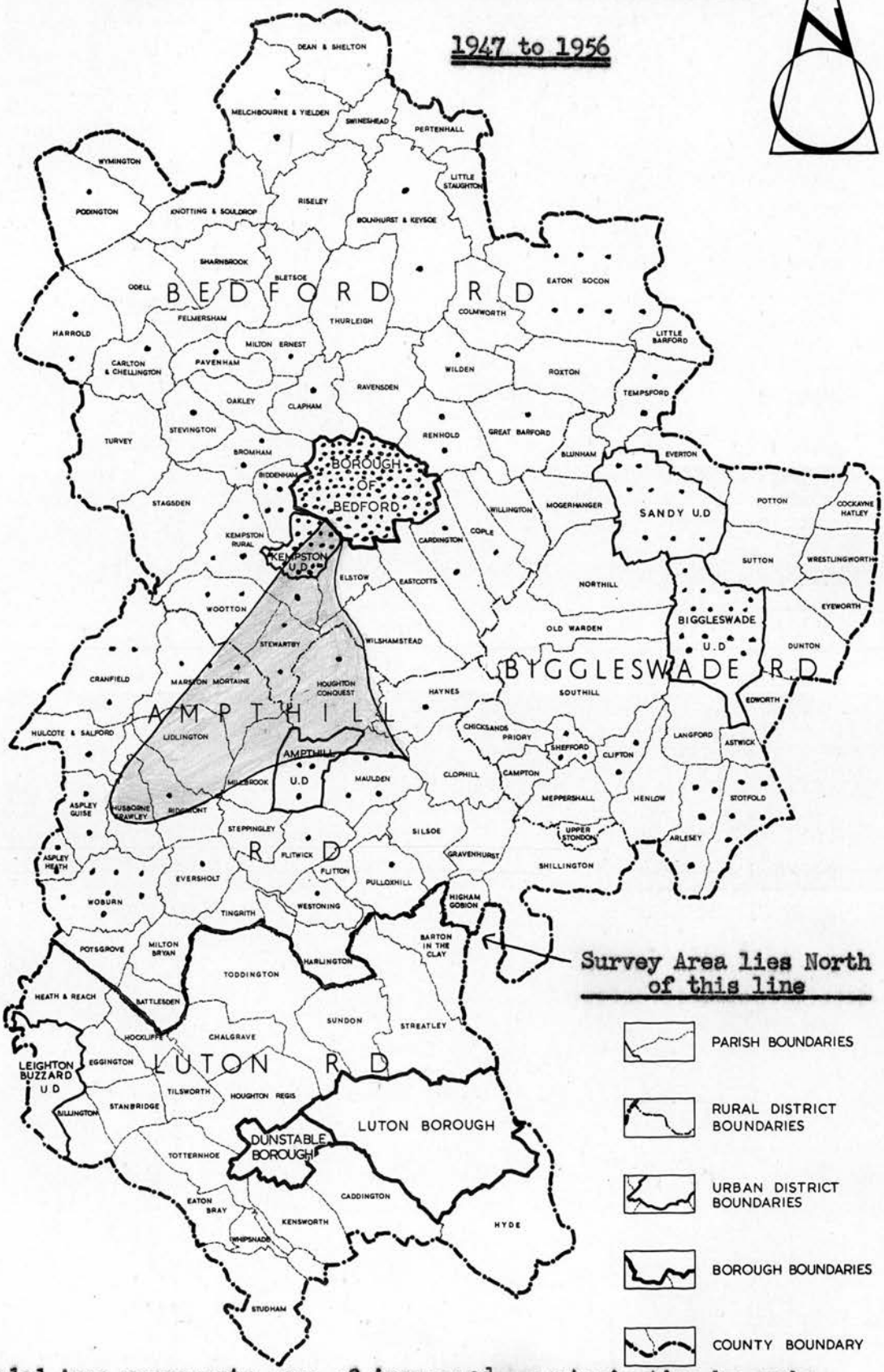
Year.	Number of patients histologically confirmed each year. No.	Percentage of total patients seen each year. %
1947	2	100
1948	6	46
1949	18	90
1950	25	78
1951	21	72
1952	28	72
1953	27	79
1954	29	78
1955	34	81
1956	27	63

BEDFORDSHIRE

ADMINISTRATIVE AREAS

MAP SHOWING DISTRIBUTION OF CASES OF LUNG CANCER

1947 to 1956



Shaded Area represents area of increased contamination by smoke (q.v. text).

COUNTY PLANNING OFFICER, COUNTY OF BEDFORD

TABLE 8.

URBAN AND RURAL DISTRIBUTION IN HOSPITAL SERIES BY AGE

	Urban		Rural		Total
	No.	%	No.	%	
Under 60 years	58	42.4	88	57.6	146
Over 60 years	80	57.6	65	42.4	145
Total	138	100	153	100	291

Chapter II.

A E T I O L O G Y

Carcinogenesis. Possible specific agents; radio-active ores, chromates, nickel, asbestos, arsenic, hydrocarbons, tobacco smoke. Relationship to lung scars. Bronchiolar carcinoma. Aetiological factors in the present hospital series; atmospheric pollution, tobacco smoke, social class. Tables 9 - 11;

Carcinogenesis.

The immediate influence which alters the life pattern of a living cell and induces the uncontrolled multiplication which characterises the neoplastic growth has, so far, resisted accurate determination. Numerous theories have been propounded, for example that of Green (1954) and Green, Wakefield and Littlewood (1957) who ascribed the neoplastic change to the

loss of tissue-specific antigen(s). He has supported this immunological theory with some clinical evidence but proof of any such proposition requires the most extensive clinical and bio-physical investigation. Similar proof is needed by those, such as Holman (1957) who believe that the key to the problem lies in the interference with the cellular catalase-peroxide system. There are also those who believe that some members of the human race are genetically "cancer-prone" and are destined to develop a neoplastic growth, the effect of some carcinogenic agent being merely to determine the site. Carcinogens have been shown to act directly on the cell nucleus but changes have also been noted in the cytoplasm and surface of the cancer cell.

Whatever the immediate cause of this cellular overgrowth it is possible that there is some carcinogen which affects the bronchial epethelium to produce a lung cancer. Whether this agent is brought into contact with the bronchi by an endogenous route or by inhalation may be the subject of argument. With regard to inhaled agents there are a number of substances used or produced in certain industrial processes which have been incriminated as carcinogens in that workers in these industries suffer a higher incidence of lung cancer than the general population.

Possible Specific Agents.

Radio-active Ores.

In the 16th century Agricola (1556) and Paracelsus (1567)

described a common lung condition which occurred among miners in the Erzgebirge in Saxony. It was not until 1879 that Haerting and Hesse showed this to be bronchial carcinoma and it was, at that time, responsible for 75% of deaths of miners in the area developing usually after about twenty years in the mines. These mines at Schneeberg and Joachimstal are now known to contain ores with a high degree of radio-activity. Arsenious oxide has been considered the possible cause but no arsenic could be detected in the urine, hair, nails or lungs (Pirchan and Sikl, 1932; Zeil, 1935). An excessive lung cancer attack rate has not been found among the miners of the nearby Johann Georgenstadt region, where the mines have a low degree of radioactivity (Hueper, 1955a). There are no reports yet of unusual mortality from lung cancer among uranium workers in Canada, Norway or the Congo, (Ringertz, 1955) but exposure has been short. Radio-active potassium, found in tobacco smoke, has also been mentioned as a possible agent (Cook, 1957).

Chromates and Nickel.

A number of surveys of workers in the chromate producing industry have been carried out showing an increased incidence of lung cancer among these persons. In Great Britain, three factories producing chromates were studied by Bidstrup and Case (1956) who found the incidence considerably higher than that expected from the age, sex and habits of the employees. Mackle and Gregorius (1948) noted an incidence 15 to 40 times as high as expected in the U.S.A. Similar figures have been

observed in certain nickel refining processes (Hueper, 1955b).

Asbestos.

The increased incidence of lung cancer among workers in the asbestos industry has been noted on several occasions. Doll (1955) found the incidence ten times that of the general population; the majority of cases occurred in association with asbestosis. The incidence of cancer diminished after the introduction of regulations for dust suppression. It may be argued that these facts are insufficient to incriminate asbestos dust itself as possessing inherent cancer producing properties. Some other agent might be present in the polluted air, and no comment was made of the smoking habits of the group studied. Furthermore, as Doll pointed out, asbestos particles affect the pulmonary connective tissue so why they should affect the epethelium as well was not known. Similar findings were noted by Bonser, Faulds and Stewart (1955) in a study of asbestos textile workers.

Arsenic.

Protagonists of the theory that arsenic is the most likely agent responsible for lung cancer point out that in those environments containing supposedly carcinogenic materials, arsenic in some form is usually also present. This applies to processes involving ore-extraction, to atmospheric pollution and to cigarette smoke.

Reported lung cancer rates vary in areas where ores with

a high arsenic content are worked. They are high in some parts of the U.S.A. and low in Sweden (Ringertz, 1955). Support for arsenic in this context was claimed by Hill and Faning (1948) who studied the workers employed in the manufacture of sheep dip. The mortality rate for cancer was twice as high among the workers handling arsenic as in the rest of the population, and this difference was due entirely to cancer of the lung and skin.

Hydrocarbons.

Atmospheric pollution by cancer producing substance(s) has been proposed by many workers as a satisfactory explanation for at least part of the widespread incidence of lung cancer. The fact that the condition is commoner in areas where atmospheric pollution is higher supports their contention. Many studies have been carried out in the last twenty years pointing out the difference in urban and rural death rates. These were surveyed by Stocks (1954) and included that in which the incidence was found to vary even in the enormous smoke polluted area of London where the highest rates were found down wind from the worst smoke producing districts. Coal tar derivatives including the aromatic hydrocarbon 3.4-benzpyrene have been shown to produce skin cancers when painted on certain experimental animals and this particular substance was identified in soot (Goulden and Tipler, 1949) and in smoke (Waller, 1952; Cooper, 1954). Aromatic hydrocarbons including 3.4-benzpyrene have been identified from other sources than soot and coal smoke, such as the exhaust gases from petrol and diesel vehicles and stationary gas engines. Kotin, Falk and

Thomas (1955) showed by biological studies that diesel smoke was carcinogenic, though Commins, Waller and Lawther (1956) found the concentration of 3.4-benzpyrene to be no higher in a large London omnibus garage containing running engines than in the open air. Whether 3.4-benzpyrene is the only potent coal tar fraction has not been proved and a number of derivatives have been found, for example, in the atmosphere of Los Angeles where no coal is burnt (Falk, Markul and Kotin, 1956). Whether these substances can produce the same effect on the human bronchial epithelium as on the skin of a mouse is not subject to direct experimental trial and there is evidence that the soot found in the lungs of town dwellers retains its benzpyrene in a firmly bound innocuous state (Cook, 1957). It is certainly oxidised by light but not so rapidly when adsorbed on to soot. Unburnt coal dust is itself not harmful from this aspect according to the studies of James (1955) who found the mortality rate of lung cancer among South Wales coal miners was less than in a similar group of local non-miners. If atmospheric pollution were the main factor, persons exposed to highly polluted air might be expected to have a high incidence. This was not found among New York policemen but Kennaway (1953) found an above average rate for motor drivers and asphalters in this country and a very high rate in gas stokers. On the other hand, smoking habits were not strictly analysed in drawing these conclusions and Reid and Buck (1956) found, contrary to expectation, that there was a normal incidence among workers in the National Coal Board's Coking Plants in 1949-54.

A further suggested source of air pollution by these hydrocarbons or other agents is the dust rising from tarred

road surfaces, also from the carbon black included in motor tyres which is liberated by wear. One objection to these being the major aetiological agent is the difficulty of explaining the sex difference in lung cancer incidence.

Other agents to which carcinogenic action has been ascribed include petroleum, isopropanol and beryllium (Hueper, 1955c).

Tobacco Smoke.

In 1928 Lombard and Doering studied the habits, characteristics and environment of individuals with or without cancer. This is probably the first study on the smoking habits of persons in relation to cancer and they found cancer rates generally higher among smokers. Lung cancer was, however, not specifically mentioned and not until 1950 was interest in this connection universally stimulated when Wynder and Graham produedd statistical evidence supporting the view that there was a definite connection between the incidence of lung cancer and tobacco smoking. The association was closer in patients with squamous growths than with adenocarcinomata. Doll and Hill (1950) came to the same conclusion. Since then, a considerable literature has appeared on the subject. It is the contention of the protagonists of the "Smoking theory" that the increase of lung cancer is largely, if not wholly, real and that it is in accord with the belief that the inhalation of tobacco smoke, particularly from cigarettes, over a period of time can produce or predispose to bronchial carcinoma. This exposure has to be continued for an unknown number of years, probably

twenty at least, and the greater the number of cigarettes smoked per diem the higher the risk of carcinoma. There is no doubt that in Great Britain cigarette smoking has increased in the last half century. In 1870 practically no cigarettes were smoked whereas in 1956 approximately 15 out of every 20 men and 8 out of every 20 women smoked, the men an average of 15.5 cigarettes per diem and the women 8. It has been calculated that there are probably 1½ million heavy (more than 20 cigarettes per diem) smokers in this country. Thattobacco tar can be carcinogenic was shown by Graham, Wynder and Croninger (1952) and other workers by animal experiments. Others have failed to confirm this, and in any case the comparison of results obtained by painting tobacco tar on to the skin of mice and the effect of tobacco smoke on human bronchial epethelium may be quite unjustifiable. Cooper, Lindsay and Waller (1954) and Seelkopf (1955) have isolated 3.4-benzpyrene from cigarette smoke and the presence of other hydrocarbons is being currently confirmed.

Considerable theory and some experimental work has been expended on the disposal of inhaled smoke. Macklin (1956) summed up the general argument that fine particles of smoke from tobacco or from the atmosphere, are inhaled to the small bronchioles and alveoli and are wafted back by ciliary action and mucus movement, thus causing a higher concentration of the contaminant in the major bronchi. Hilding (1957) has studied extensively bronchial ciliary action and concluded that there

were points of comparative stasis in the ciliary stream and these points were more apt to be the site of a growth. Why the buccal and tracheal mucous membranes remain comparatively free of carcinoma has not been adequately explained. Auerbach, Gere, Forman, Petrick, Smetlin, Muesam, Kassoury and Stout (1957) in a detailed histological study of bronchial mucous membrane in cases of bronchial carcinoma and other conditions concluded that irritation by cigarette smoke was a major factor in the production of lung cancer.

Direct experimentation on humans being impossible in this condition, evidence to support the "Smoking theory" must be sought indirectly and two types of survey have been used. The retrospective studies involve the analysis of case records of persons certified as dying from lung cancer and comparing these with suitable control cases. Stocks and Campbell (1955) are engaged on such a study in N.W.England at present and provisional results would agree with the hypothesis that atmospheric and tobacco smoke are important factors. The prospective studies, such as those being carried out by Doll and Hill (1954, 1956) on British Doctors and by Hammond and Horn (1954) in America, both consist of studying the deaths occurring in a group of persons all living at the start of the survey. These studies indicate that the incidence of lung cancer rises parallel with the number of cigarettes smoked. For example, in Doll and Hill's study of British Doctors, the death rate for lung cancer rises per year 0.07 per 1,000 in non-smokers and 1.66 per 1,000 in heavy smokers. The figures

for light cigarette smokers and for pipe smokers lie between these two extremes as does the figure for those men who have given up smoking. The incidence of carcinoma in sites other than the bronchus was 2.02 and 2.04 per 1,000 for smokers and non-smokers respectively a fact which, it is claimed, refutes the argument that smoking merely determines the site of growth in persons destined by genetic factors to develop it somewhere.

It has been found in the majority of these surveys, of either type, where records of the histological types of tumour are available that any association between the smoking history and development of lung cancer applies only to certain tumour types. Thus Wynder and Graham (1950) found the epidermoid tumours had such an association but it was less apparent with adenocarcinomata. Doll, Hill and Kreyberg (1957) found in men a close relationship between the daily amount smoked and the development of squamous, large cell and small cell carcinomata (including oat cell and anaplastic growths) but only slight, if any, relationship with the development of other histological types, principally adenocarcinoma and bronchiolar carcinoma. No conclusion was drawn from a study of women as the number of patients was too small. These findings are in accord with the work of Kreyberg (1955) in Norway. Ringertz (1955) surveying reports from many European countries, U.S.A. and Japan, from 1931 to 1953, found that the male/female ratio in adenocarcinoma varied from 0.69/1 to 1.89/1 whereas for squamous cell growths the ratio varied from 6/1 to 10/1. Even allowing for some errors of interpretation it is obvious that there exists some

difference in causation between these two types of growth.

Various authors have elaborated objections to the "Smoking theory" frequently on the grounds of bias in the control series (Kraus, 1954) or methods of selection of series (Berkson, 1955), or conclusions drawn from the material analysed (Hueper, 1955d; Fisher, 1957).

The statistical evidence incriminating smoking as a major factor is stronger than the experimental as conflicting results are obtained by animal experiments using coal tar preparations, tobacco smoke extracts or smoking machines. Those who believe that arsenic is the main carcinogenic agent are supported by the fact that cigarettes contain an appreciable quantity of this substance. Virginian tobacco which has largely ousted eastern European "Turkish" type tobacco in world wide consumption contained a much higher proportion of arsenic. Owing to recent abandonment of arsenical insecticide sprays, tobacco now contains much less arsenic; for example, in one popular English cigarette it has dropped from 25 - 100/ug. per cigarette in 1948/9 to 1 - 2/ug. in 1956 (Bailey, Kennaway and Urquhart, 1956). It is not possible to use the evidence of a comparatively low incidence of lung cancer among peoples who for religious reasons do not smoke tobacco to support the tobacco theory of causation. The environment of these peoples, such as Mohammedans, differs in many respects from that of caucasian peoples and the lower standards of diagnosis and recording of deaths render such comparison largely valueless.

Relationship to Lung Scars.

There has been considerable speculation on the relationship between scarring or fibrosis in the lungs and lung cancer. As mentioned earlier several groups of persons who appears to have an elevated cancer rate due to inhalation of a dust, such as asbestos workers and Cumberland iron-ore miners, also suffer from pulmonary fibrosis. Interest was focussed on this point when Raeburn and Spencer (1953) published their findings of a study of very early lung cancers discovered at autopsy. Eleven of the growths were found in association with scars situated near the lung periphery. Although four of them showed features resembling the carcinoid type of malignant adenoma, the authors considered them oat cell carcinomata. This appeared to conform with isolated reports of the close anatomical association between lung cancer and the scars of healed tuberculosis or bronchiectasis. Woodruff and Nahas (1951) in discussing cases of associated tuberculosis and cancer postulated that healed tuberculosis commonly led to bronchiectasis where normal columnar bronchial epethelium was transformed into a squamous type, a transformation which often preceeded squamous cell carcinomatain other organs. In addition the bronchiectatic saccules might be points for accumulation of tobacco tar. Bryson and Spencer (1951), however, found in a large autopsy series only four examples of carcinoma arising in the walls of a bronchiectatic cavity. It was reported in the United States Conference on the Chemotherapy

of Tuberculosis in 1956 that a study of five cases of lung cancer arising in 3,300 cases of pulmonary tuberculosis treated with prolonged chemotherapy suggested that the growths originated in squamous metaplastic bronchial mucosa at the broncho-cavitary junction.

Gelzer (1956) studied at the Basle Institute of Pathology 539 cases of lung cancer. About half of the peripheral tumours were situated in the neighbourhood of a scar, mostly from tuberculosis but some from infarction. In spite of this he was doubtful about the connection and evidently did not consider a causal relationship to be proven. Evans (1956) in his chapter on bronchial carcinoma doubted if the evidence produced by Raeburn and Spencer justified the conclusions that have been drawn from it. He considered that the histological features of the peripheral growths described resembled more closely those of bronchial adenoma than of carcinoma and the fact that four out of five were in women tended to confirm this. He also criticised a previous study of Peterson, Hunter and Sneeden (1949) who described five cases with minute lesions considered to be early carcinomata. Again four of these growths were in women, two had been treated for carcinoma of the large bowel and four had evidence of localised bronchiectasis. He considered that to date the study of minute areas of atypical metaplasia have not proved helpful in assessing the origins of lung cancer.

Further work by Raeburn and Spencer (1957) is more convincing, however, and they stated that about one quarter

of lung cancers were related to scars from previous lung damage. The fact that terminal bronchioles, unlike large bronchi, can proliferate during life allows a possibility of neoplastic development in the periphery of the lung. The majority of cancers found in relationship to scars are adenocarcinomata but all varieties have been found. The authors account for the fact that centrally placed growths are not associated with scars by the belief that many of these growths are in fact secondary to a more peripheral primary cancer which has spread to the regional glands and thence back along the bronchi.

There are periodic reports, however, of patients who are found to have areas of malignant tissue discovered usually accidently when an autopsy or resected specimen is histologically examined. These tumours resemble in several aspects the basal cell carcinoma of skin (Bowen's Carcinoma) and are frequently associated with bronchiectatic change in the lung (Raeburn and Spencer, 1953; Oureton and Hill, 1955). The growths can metastasise, as in the latter authors' case, but they appear to be relatively benign and are in clinical respects rather similar to the carcinoid type of malignant adenoma to be described later. One of the earliest forecasts of the increase in incidence of lung cancer was based on the theory that squamous metaplasia may be the initial step in the genesis of squamous carcinomata. This was made by Winternitz, Wason and McNamara in 1920 in their publication on the Pathology of Influenza. They observed that

squamous metaplasia was a common occurrence in post-influenzal pneumonia and they considered that the large number of such cases following the 1918-19 influenza pandemic would result in an increasing incidence of lung cancer after a latent developing period. Although the forecast was correct, it is difficult to accept their theory of causation as it fails to explain the marked difference in sex incidence and also the fact that the population of Iceland, for example, who suffered heavily from the pandemic started an increase in lung cancer rates long after Western Europe and the U.S.A.. There were other influenza epidemics in 1922, 1924, 1927, 1929 and 1933 but all less than 1/7 of the 1918 epidemic in terms of mortality (Stocks, 1953). If Virus A had been the cause of lung cancer the incidence should surely have diminished by now. Thus, although influenza cannot be completely excluded from the list of possible causes it cannot be of great importance.

Bronchiolar Carcinoma.

Whether this form of lung cancer has the same aetiology as the more common forms is uncertain. It comprises such a small proportion of the total incidence that it has not been practicable to assess the role of possible aetiological factors. The histology most closely resembles adenocarcinoma which, as has been shown, bears little relationship to smoking and, like it, has a sex ratio of unity. Morphologically it resembles jaagsiekte (drive sickness) a virus disease affecting sheep in various parts of the world,

particularly South Africa, described in a report by the African Expedition of the Rockefeller Institute for Medical Research. This was once thought to suggest a virus aetiology for lung cancer generally but no virus which has any claims to be responsible has ever been recovered from man. Dungal (1951) in a review of lung cancer in Iceland stated that jaagsiekte was common there but only three cases of human lung cancer had any histological similarity and all three were town dwellers. A further interesting point is that no bronchiolar carcinoma had been found among the radium ore miners at Joachimstal (Pirchan and Sikl, 1932). Thus there is even less certainty about the cause of this particular form of cancer than of the other varities but it would seem likely that its causation may be allied to that of adenocarcinoma of the lung.

Aetiological Factors in the Present Hospital Series.

Atmospheric Pollution.

There are no industries in the area concerned with the smelting of chromate or nickel ores or the manufacture of arsenical products. All the area is subjected to a degree of smoke pollution from domestic and industrial sources. The major smoke producing industry is brickmaking, the works being situated in the west of the area. The Map (following Chapter I) shows a shaded area in which it was shown by Blakemore, Bosworth and Green (1948) that the quantity of fluorine on pasture was very much greater than in the rest of the county.

The area is below the brick-works judged from the prevailing wind and as the fluorine was derived from their chimney smoke it is reasonable to assume that the ground level concentration of other constituents of smoke was also higher in this area. The mortality rate for lung cancer in this area of higher smoke concentration is not above that for other rural districts in the area but the number of cases is very small.

The urban/rural ratio (1.3/1) of patients attending the hospital is of no significance in studying causes as it might be due to more use being made of the hospital by the urban population.

The greatest traffic stream in the area passes north and south near the eastern boundary where lies the trunk road A.1. The Map shows an aggregation of cases in this area, but this cannot be attributed solely to atmospheric contamination by motor vehicle exhaust gasses as the area contains several centres of population scattered along the road.

Tobacco Smoking.

A tobacco smoking history was obtained from 132 patients, 45.5% of the series as a whole; this included 47% of the urban patients and 44% of the rural. Table 9 shows the distribution of smoking habits; heavy smoking implies the consumption of at least twenty cigarettes per day for at least twenty years, light smoking below this level. It must be mentioned that large scale surveys of smoking habits involve considerably greater accuracy in obtaining details

than has been employed here and no special questionnaire has been employed as is essential for reliable results. Among those with recorded smoking histories the number of women is so small (9 patients) that no conclusions can be drawn from an analysis. Among the men 60% were heavy smokers, 30% light smokers, 7.6% pipe smokers and only 2.4% were non-smokers. This is in accord with numerous series which record the high percentage of heavy smokers among lung cancer patients. In only 78 patients were both the smoking history and the histological typeof growth recorded and these are shown in Table 10. The fact that 59% of the squamous growths and 60% of the undifferentiated growths were heavy smokers is in accord with many other reports but it is interesting to note that of the 9 adenocarcinomata 7 were heavy smokers, the other 2 being light smokers. This is completely at variance with reports already quoted on this association but the numbers concerned here are very small. It is possible that a bias exists in the recording in clinical notes of smoking histories, and the non-smoking habit might not be entered whereas the smoking habit be entered. This bias should, however, apply to all histological groups.

Social Class.

Table II sets out the incidence among the 209 patients who could be classified into the five Social Classes as defined by the Registrar General. It can be seen that the incidence is fairly even in the first three Classes but is definitely higher in Classes IV and V, groups comprising

mainly labourers and unskilled manual workers. Standardised lung cancer mortality rates for these Classes in England and Wales as quoted by the Registrar General in his Occupational Mortality Investigation of 1950 (1954) are also shown. A similar gradient is noted except that Social Class III is proportionately higher than in this series. The findings of Brett, Benjamin, Craig and Freeman (1956) among Islington men picked up by Mass Radiography are also shown. They noted a significant elevation of incidence in Class V. This relative frequency of lung cancer in the lower Social Classes may be due to different smoking habits or different exposure to atmospheric pollution or to some other factor. There is also the possible bias in this series and that of Brett et al that members of the Social Classes I and II are less likely to attend general hospitals or Mass Radiography Units and more likely to be seen in private consultative practice. The Registrar General's figures should be free of this bias, however, as they are based upon death certification.

TABLE 9.

SMOKING HABIT BY SEX.

		Men	Women	Total
Total in series		257	34	291
Smoking habit recorded		123	9	132
Smoking habit	Heavy	73	2	75
	Light	37	1	38
	Pipe	10	-	10
	None	3	6	9

TABLE 10.

SMOKING HABIT BY TYPE OF GROWTH. MALES ONLY.

		Squamous		Undifferentiated		Adenocarcinoma	
		No.	%	No.	%	No.	%
Smoking habit	Heavy	29	59	12	60	7	78
	Light	17	35	5	25	2	22
	Pipe	1	2	3	15	-	-
	None	2	4	-	-	-	-
	Total	49	100	20	100	9	100

TABLE 11.

INCIDENCE OF LUNG CANCER BY SOCIAL CLASS.

Author	Social class I	II	III	IV	V
Present series. Rate per 1,000	3.2	2.9	2.9	5.2	4.1
Brett et al. " " "	-	1.45	2.8	2.6	6.3
Registrar General. Standardised mortality ratios	80	79	108	89	116

Chapter III.

P A T H O L O G Y

Histogenesis. General pathological features; nomenclature; distribution of growths by type, site and age; squamous growths; undifferentiated growths; adenocarcinomata. Spread of tumours; incidence of metastases. Cavitation in bronchial carcinoma. The Association between atherosclerosis and lung cancer. Bronchiolar carcinoma. Malignant adenoma.
Tables 12 - 17.

Histogenesis.

A malignant neoplasm can be considered as an uncontrolled overgrowth of cells. The particular cell which is concerned in a malignant bronchial neoplasm has not been identified to the satisfaction of all histologists nor is it certain that only one basic cell type is responsible for the variety of

growths which can be produced. It is likely that the reserve cell which lies in the basal epethelium of the bronchial wall is the parent cell as it is capable of mitosis, the basic necessity for malignant change. As these cells are capable of replacing squamous or columnar epithelial cells in the bronchial epethelium it would be possible for malignant change to give rise to an overgrowth of these cell types. If the reserve cell multiplied without changing its basic undifferentiated character, the resultant neoplasm would have the same undifferentiated appearance. It is possible, however, that the different varieties of carcinoma arise from distinctly separate parent cells and reproduce the character of those cells.

General Pathological Features.

Nomenclature.

Although some bronchial carcinomata on microscopic examination show a uniform picture, it is more common for a certain amount of variation to be seen in the cell pattern. This variation has been responsible for the measure of disagreement which exists among histologists in defining the cellular appearance of bronchial growths. No firm definitions have been accepted for the description of bronchial carcinomata and so many histologists prefer their own descriptions that it is unlikely that full agreement will ever be reached.

There are certain cellular patterns, however,

which are almost universally accepted. The squamous or epidermoid growth which may vary in degree of differentiation, the more highly developed examples showing keratinization and the presence of epithelial pearls is easily recognised. So, also, the glandular tumours or adenocarcinomata which show tubule formation and most of which produce mucin. The undifferentiated group vary considerably in appearance, the most typical probably being the densely cellular, closely packed small celled variety or oat cell tumour. Not all undifferentiated tumours consist of this type of cell, and round or polygonal cells can be predominant. Hence there is a considerable variety of terms used to describe these tumours, "spheroidal", "round cell", "polygonal cell", "oat cell", and others. There is probably no difference in malignancy or clinical development between the growths so described. A further point causing confusion in terminology is the fact that, as mentioned above, different portions of one tumour can show considerable variation in cellular pattern. Thus a predominantly squamous growth can contain areas of tubule formation or a sheet of closely packed round cells suggestive of an oat cell growth. Kirklin, McDonald and Clagett (1955) for example stated that in oat cell growths the cells were never arranged in any organised pattern but Walter and Price (1955a) on the other hand, reported rosette or tubule formation in about half their oat cell growths making these resemble adenocarcinomata. Similarly, squamous metaplasia may occur in adenocarcinomata (Walter and Price, 1955a; Phillips, Basinger and Adams, 1950). This

pleomorphism was well recognised by Willis (1953).

The trend in modern writing is to describe cases under three broad histological groups, Squamous, Undifferentiated and Adenocarcinoma. The term "Oat celled" is sometimes used synonomously with undifferentiated although it is really only one variety of it. This grouping has been employed in the analysis of the present series and no attempt has been made to make more detailed histological division as I do not consider it serves any useful purpose when analysing a small number of patients in whom the histological reports have been issued by various pathologists. Although the majority of biopsy and autopsy reports emanate from one local source, reports on resected specimens come from six different pathology departments.

In addition to the three main types of growth, two other varieties of malignant bronchial neoplasm are recognised, (1) that which is commonly known as Alveolar Cell Carcinoma and (2) Metastasising or Malignant Adenoma.

Distribution of Growths by Type, Site and Age.

The proportion of the various types found in different series depends upon the source of the material. Figures from resection specimens and from autopsy series will differ from each other as some varieties of tumour are more commonly resected than others. Also, the group of persons studied may be selected as in Service personnel with restricted sex and age groupings. The country of origin, race and possible change in proportion with the passage of years may all play

a part.

A sample of figures recently published is given in Table 12 and compared with those cases in the present series in whom the histology was proved, 154 men and 20 women.

Walter and Price (1955a) stated that published series of necropsy material showed a variation in squamous growths from 6.9 to 61.2% and in clinical and surgical material from 31.3 to 75%, while the proportion of adenocarcinomata in the latter material varied from 0 to 22.7%. Nevertheless, in general terms, squamous growths probably account for about 50% of lung cancers in a general series in this country at this time, undifferentiated growths about 30%, adenocarcinomata about 15% with the other minor varieties occupying not more than 0 to 5%.

As regards the site of origin of bronchial neoplasms, they arise anywhere in the bronchial tree as far distal as the terminal bronchiole. It is interesting that tumours of the trachea are extremely uncommon although bronchial growths can extend into the trachea. Belief that the majority of lung cancers originate in major bronchi has been expressed by Davidson, Smithers and Tubbs (1951), Willis (1953) and Strang and Simpson (1953). On the other hand, Walter and Price (1955b) claimed that half of the tumours in their series originated in bronchi too small to be seen by naked eye and felt this would confirm the work of Raeburn and Spencer (1953). As has been stated in an earlier section, however, the carcinomatous nature of the tumours reported by the latter authors has been doubted.

Tables 13 and 14 show the distribution and proportion

of varieties of growth found in this and other series. In some tables, including Table 14, the following abbreviations are used. RMB for the right main bronchus, RUL for the right upper lobe, RML for the right middle lobe, RLL for the right lower lobe, LMB for the left main bronchus, LUL for the left upper lobe, LLL for the left lower lobe. It is a fact that in practically every series more growths are found in the right than the left lung but this is due to the difference in weight, and therefore, volume of the two lungs.

Table 15 sets out the varieties of growth by age groups.

Squamous Cell Neoplasms.

These can be situated in any portion of the lung, fairly equally divided between the main or major lobar bronchi and the smaller bronchi towards the periphery of the lung. A broad division into those originating in the main bronchi and those in the lobar bronchi or beyond is shown in Table 16. This shows that squamous growths constituted 53.6% of growths in major bronchi and 56% of those elsewhere. It has been the experience of many clinicians that a growth which invades the chest wall is most likely to be a well differentiated squamous growth, although 16 such cases seen at the Mayo Clinic were caused by squamous growths (6), undifferentiated (6) and adenocarcinomata (4), (Gronqvist, Clagett and McDonald, 1957). Apical tumours producing a superior sulcus or Pancoast Syndrome are usually of squamous type. In this series there were three cases showing the superior sulcus syndrome and all were caused by squamous growths.

The evolution of a squamous growth is usually slower than the other two main varieties, the duration of symptoms longer and age of onset greater. It is probably unjustifiable to claim statistical significance for figures reported by Lea (1952) for the average age of onset, anaplastic carcinoma 37.8 years and squamous carcinoma 41.2 years, as the duration of symptoms is not necessarily a true indication of the date of onset of malignancy. Necrosis in the tumour is not uncommon and abscess formation occurs much more frequently in this type than in the others (Strang and Simpson, 1953). Delarue (1955) found it responsible for all massive, excavated growths.

These growths remain localised for longer than other types and if detected, there is a better chance of finding no spread beyond intrapulmonary lymph nodes when the lung is resected. This chance is over twice as good in the report of Nohl (1956).

Squamous growths are predominantly a male affliction; in this series only 5.5% of squamous growths occurred in women, a finding similar to the 3.5% of the Mayo Clinic (Putton, McDonald and Moersch, 1951) and of Kreyberg (1954) in Norway. Putton et al stated that squamous growths seldom occurred below the age of 40 years. Comparatively few lung cancers occur below this age, however, and in this series of the 9 that did so 3 were of the squamous variety. Those occurring in younger persons do certainly tend to be of the other types (vide infra).

Undifferentiated Carcinoma.

This tends to be a highly malignant growth which has a

short history and metastasises early. The prognosis, as will be shown in a later chapter is poor. They affect the main and major bronchi more commonly than the peripheral branches (Ochsner et al, 1952). In this series, Table 16 indicates the rather higher proportion in major than in other bronchi. It is reputed to affect a younger age group. In this series 21.8% of them occurred below the age of 50 years compared with 15.4% of squamous growths. On the other hand, Delarue (1955) collected thirty five reports giving information on the age incidence of squamous and undifferentiated growths from European, North and South American and Far Eastern countries and with his own material of 672 cases found very little difference between the two types.

Adenocarcinoma.

Responsible for about 15% of all lung cancers this type, as has been shown previously, is often the commonest type occurring in women equal to undifferentiated growths in the women in this series. It has a definite predeliction for the smaller bronchi. Ochsner et al (1952), in a series of resections found 5% of adenocarcinomata in main bronchi, 44% in lobar bronchi and 55% in more peripheral bronchi. Walter and Price (1955b) found adenocarcinoma was always peripheral in those growths whose origins they could definitely locate, but their series was also of resected specimens only. Table 16 shows that, in this series, only 7% of tumours in major bronchi were adenocarcinomata compared with 14% of tumours arising

distal to the major bronchi.

Necrosis and cavitation in this type of growth is uncommon. Spread can occur early and rapidly and the degree of malignancy is comparable to that of undifferentiated growths.

Spread of Tumours.

Lung cancers spread (1) by expansion of the primary growth to include more and more of the surrounding lung and contiguous structures, (2) by lymphatic channels, first to the intrabronchial nodes and thence to the hilar and mediastinal glands, (3) by vascular channels and (4) possibly by tumour emboli via the lumen of the bronchial tree.

(1) This is obvious in many cases and is commonest in squamous growths.

(2) Lymphatic spread is unfortunately present in many patients by the time resection is performed. Nohl (1956) has reported a detailed analysis of the mode of lymphatic spread from the various lobes of each lung. Such spread is mainly upwards, and in the left lung drainage often occurs up the right paratracheal chain of glands. Both the submucous lymph channels and the peribronchial channels may be involved without gross changes being noted on bronchoscopy. Submucous lymph spread may carry a growth over the carina into the other lung. In Nohl's series of 100 resected lungs, 75 showed lymph node involvement and he quoted 31 to 70% occurring in other authors' series. As will be discussed later the prognosis after operation depends largely on the degree of

regional node involvement. Regional nodes are more frequently involved in the early stages of undifferentiated growths than of squamous growths.

(3) Cudkowicz and Armstrong (1953) found that in 4 out of 5 bronchial carcinomata studied dilated lacunae derived from bronchial arteries were seen in the tumour, together with diffuse, proliferative bronchial artery anastamoses. This was similar to the findings reported earlier by Wood and Miller (1938). This might make the vessels more liable to invasion by the malignant growth. Distant blood borne metastases are commoner in the undifferentiated tumours than in the squamous variety but differences in the local vascular pattern between one variety and another have not yet been reported. Undifferentiated growths, however, quite commonly involve the adventitia of the aorta (Tanner and Gordon, 1952), and by tumour emboli spread to the pancreas and adrenals via the coeliac axis and other aortic branches. Cerebral metastases probably arise from blood borne tumour emboli entering the pulmonary veins. In Nohl's series, vascular involvement had occurred in 23.7% of squamous growths and 40% of undifferentiated growths and he quoted published series of overall vascular involvement varying from 30 to 60%.

(4) Intrabronchial aspiration of tumour cells from one bronchus to another must occur as the surface cells of a bronchial carcinoma are very liable to be shed and can often be detected in the sputum. That clumps of neoplastic cells are capable of instituting a secondary focus of growth is certainly true for intra-vascular spread but it has not been

conclusively proved that intrabronchial spread takes place in the common forms of lung cancer. It has been claimed to occur in bronchiolar carcinoma, as will be described later, but this may not be a justifiable parallel.

One argument against such aerial spread is the comparative rarity with which secondary deposits are found in the other lung of a patient with even advanced lung cancer, in whom lymphatic and vascular channels have disseminated the growth widely throughout the rest of the body. Ryan, McDonald and Claggett (1957) reported finding evidence of carcinoma in the "good" lung of 12% of patients with lung cancer even though the bronchi of the "good" lung appeared normal on macroscopic examination. They studied the thickness of bronchial mucous membrane and found that the epethelium proximal to a bronchial growth and in the "good" lung tended to be thicker and present a higher incidence of squamous metaplasia, much of it atypical, than the normal bronchial epethelium. Obviously much must depend in this type of study on the interpretation of squamous metaplasia and the earliest evidence of neoplasia. No mention was made of submucous lymphatics being involved with growth but if lymphatic spread from the primary growth was indeed absent, a theory of multicentric origin must be accepted. This, however, is not borne out by clinical or post-mortem experience which supports the belief that a lung cancer arises from only one site somewhere in the bronchial tree.

Incidence of Metastases.

Sixty eight post-mortem records are available for patients in this series. The incidence of the major metastases are shown in Table 17. Very few patients had no metastases at all but seventeen of them (25%) had no extra-thoracic metastases reported. The incidence will depend considerably on the time and trouble expended by the pathologist; metastases in organs such as the liver and spleen will be recorded but many bone secondaries will pass unnoted if they have not been evident clinically. Miyaji et al (1955) in a pathology survey of 406 collected bronchial carcinomata in Japan found only 2 without metastases. Their findings and those of Ochsner and DeBakey (1942) in a collected series of 2,579 cases are also given in Table 17.

Galluzzi and Payne (1956) in a study of 741 lung cancer autopsies found cerebral secondaries in 26 to 30%. They were most common from undifferentiated and adenocarcinomatous growths than from squamous growths. In this series, they were present in 32% of cases and were more than twice as common in the undifferentiated group as in either of the others but the incidence in the squamous group was equal to that in the adenocarcinomata. This may be due entirely to chance.

It is evident that (1) metastases are almost universal in patients dying from bronchial carcinoma, (2) extra-thoracic metastases are present in about 75% of such patients, (3) that extra-thoracic metastases occur in the squamous, adenocarcinoma and undifferentiated groups in ascending order of frequency, with the last group much the most widely affected, (4) that suprarenal secondaries differ from others in that they occur

commonly in all three groups and are, in fact, one of the commonest sites for extrathoracic metastases.

Cavitation in Bronchial Carcinoma.

Bronchial carcinoma presents a cavitated appearance in anything from 12 to 29% in post-mortem material, the proportion being lower in series of a general nature than among those patients referred to a thoracic surgical unit (Brock, 1948). Strang and Simpson (1953) found radiographic evidence of cavitation in 3.6% of 1,930 lung cancer patients. In the present series cavitation was seen radiographically in 12 patients, 4.1% of the total.

The two methods by which cavitation commonly forms are (1) bronchial obstruction by growth, causing inflammatory changes to develop in the segment distal to the obstruction with consolidation and then liquefaction and abscess formation; and (2) the actual necrosis of a tumour mass. The first type is really a non-specific effect of any bronchial obstruction and can therefore result from any of the histological varieties of growth. The second type probably develops as a result of the tumour mechanically comprising its own blood supply and in the majority of cases occurs in a squamous carcinoma. While most neoplastic lung abscesses are thick walled with irregular inner surfaces, often presenting a scalloped appearance, the contents may be coughed up leaving only a thin cavity wall. The radiographic resemblance to tuberculous cavities or even cysts can then be striking.

This confusion with tuberculosis or simple lung abscess is increased by the fact that in the series of Strang and Simpson the most frequently involved segments were the posterior segment of the upper lobes and apical segment of the lower lobes which are commonly involved in other diseases.

In this series, of the twelve cases with cavitation four were caused by squamous growth, four by undifferentiated and in four the histology was not known. Six growths were situated in the upper lobes, four in lower lobes, one in a main bronchus and in the last the site could not be determined. Anderson and Pierce (1954) reported six cases of bronchial carcinoma presenting radiographically as thin walled cysts. These cysts had a smooth wall, did not contain fluid and had no surrounding consolidation. All were due to squamous growths and the authors believed the tumour cells grew into, and lined, the wall of a pre-existing cavity. The clinical course and prognosis was the same as for any other peripheral carcinoma. The authors did not state the incidence of these thin-walled cavity tumours but they are uncommon and obviously not easy to diagnose.

The Association between Atherosclerosis and Lung Cancer.

It was originally reported by Wanscher et al (1951) that atherosclerosis occurred less commonly in cases of cancer of all types than in non-cancerous individuals. In a series of 501 cases, Lea (1952) studied this in relationship to bronchial cancer and confirmed the negative correlation. The

The significance of this finding has not, so far, been accounted for. No special attention has been paid to this point in those cases coming to autopsy in this series but a review of the autopsy reports indicate that atheroma of a moderate or marked degree was reported present in over one third of the cases. This is at variance with the reports noted above but as a great deal would depend on the standards and definitions employed, no definite conclusion can be drawn.

Bronchiolar Carcinoma.

This variety of neoplasm differs in several respects from the three main histological types of lung cancer. The characteristic histological picture is the lining of alveoli and terminal bronchioles by cuboidal or columnar cells with mainly eosinophilic cytoplasm and rare mitotic figures. Mucin secretion is common. These cells line apparently unaltered alveolar septa. The origin of these cells is disputed. Geever, Neubuerger and Davis (1943) are protagonists of the theory that the alveolar wall ground substance contains mesenchymal cells which proliferate under various stimuli and appear in a variety of pulmonary diseases and their degree of multiplication and development can extend to a malignant condition. These authors would favour the term, "Alveolar Cell Carcinoma". Other authors, such as Storey, Knudson and Lawrence (1953) who have presented the most comprehensive survey of the condition, consider that the cells are derived from the bronchiolar epethelium and not from the alveoli.

This view is shared by Spencer and Raeburn (1956) who found when examining lung scars discovered during routine autopsies that bronchiolar epithelium can grow into, and line, damaged alveoli. Such authors would favour the term, "Bronchiolar carcinoma". The third name by which this condition has been described, "Pulmonary Adenomatosis" suggests a benign process. The duration of life in some patients with this condition has been considerably longer than is usual in malignant growths of the lung and it has been suggested that some of these patients are in fact suffering from a benign and not a malignant condition. The term "Pulmonary Adenomatosis" would be justified in such cases but as the histological picture may be exactly the same in other patients who show spread of the growth to regional lymph glands and other organs, it is impossible to say which growths are truly benign and which malignant. This term could well be abandoned in favour of one or other of the more descriptive titles.

The differentiation from adenocarcinoma can be difficult as the histological pictures may be very similar. Involvement of larger bronchi would favour a diagnosis of adenocarcinoma in equivocal cases but exact differentiation may be impossible as in a case of a peripheral tumour resembling bronchiolar carcinoma but where small bronchi were invaded, reported by Hanbury and Hill (1956). Certainly growths occurring primarily in major bronchi can be ruled out as bronchiolar carcinomata as these consistently begin peripherally and there is constant absence of involvement

of major bronchi (Storey et al, 1953).

With regard to gross pathology, the growth shows a marked degree of variability. The two commonest appearances are (1) widespread, discrete nodulation of one or both lungs, each involved area showing typical tumour growth though there may be slight variations from place to place and (2) a more homogeneous mass of variable size, which possibly arises from the coalescence of innumerable involved alveoli. Of the 205 cases reported by Storey et al 26% presented first with a single peripheral nodule, over 66% were confined to one lung at that time and only 20% showed widespread, bilateral nodules. In the four cases in the present series, three were of the coalescent type, in two of whom areas of tumour were also found in the other lung, and the fourth presented with disseminated bilateral nodules. It is interesting that the first recognisable description of this condition has been ascribed to Malassez's (1876) account of a case with "Multiple nodular encephaloid carcinomata in the lung" (Spencer and Raeburn, 1956). Spread of the tumour is by the recognised routes. Lymphatic invasion of the lung was demonstrated in over 50% of the series of Storey et al and 38% of them had intra-thoracic lymph nodes involved. They also found that 15.6% showed distant metastases indicating frequent blood borne spread, and also a number of cases showed nests of tumour cells lying in the bronchial lumen which might possibly be a source of aerial spread.

Decker (1955) surveying a somewhat overlapping series concluded that metastases occurred in 45% of cases and these were via the lymphatic and blood streams. Herbut (1946 a, b) strongly favoured the theory of a unifocal origin for these tumours, breaking off of papillary processes then developing and by intra-bronchial spread disseminating the growth through the lungs. Hutchison (1952) also considered this quite probable and claimed that as these tumours could be extremely slow growing, this theory could explain the occasional appearance of foci in the opposite lung after pneumonectomy. Such appearance after resection has been claimed by protagonists of the theory of a multicentric origin to prove their point. No blood borne metastases were found in the four cases in the present series; regional glands were not involved in two cases but both of the others had tumour tissue in regional and supra-clavicular glands. The age incidence of patients with bronchiolar carcinoma is the same as for lung cancer generally but the sex ratio is about equal, as it was in the present series. The overall incidence varies from 0 to 5% of all lung cancers in reported series, 1.4% in the present series.

Malignant Adenoma.

There are a number of tumours reported in the literature which arise from the bronchial wall and have a macroscopic appearance similar to, often indistinguishable from, benign bronchial adenoma. The histological appearance, however, is different and so is their effect on the patient as a degree

of malignancy exists in them which, although not equal to that of true bronchial carcinoma, is certainly not found in the simple adenoma. These tumours have become known as "malignant adenomata" although this is a contradiction in terms and would be better abandoned in favour of a less ambiguous title, such as those of its two varieties. These tumours arise, most probable, from the mucous glands in the bronchial wall (Willis, 1953). There are two histological varieties, the carcinoid and the cylindroma. There were very few cases of the cylindromatous variety reported in this country until Belsey and Valentine (1951) drew attention to it, since when several reports have appeared.

The carcinoid bears a superficial resemblance to the argentaffinoma (carcinoid) of the intestine and consists of uniform polyhedral cells arranged in groups separated by a vascular stroma. It tends to be centrifugally situated in the lung and is rarely found in the trachea or near the carina. It is the commoner of the two varieties forming 85% of malignant adenomata (Liebow, 1951). Extrathoracic metastases are not uncommon, the liver being a frequent site.

The cylindroma has an acinar arrangement with deeply staining cells of varying size; mitoses are seen and mucin secretion is invariable. It is usually centrally situated in the lung.

The sex incidence is roughly equal and they are commonest in the 30 - 40 years age group but can occur at any age. In this series one patient was a woman of 38 years

who had a cylindroma in the left upper lobe bronchus and the other a man of 70 years with a carcinoid growth in the right lower lobe. The first patient had metastases in the liver and the second in the pleura.

The possibility that these tumours may become frank carcinomata has been suggested by several authors, such as Price-Thomas (1954) in a review of benign tumours of the lung.

TABLE 12.

DISTRIBUTION OF HISTOLOGICAL TYPES. PRESENT SERIES AND OTHERS.

Author	Ochsner et al (1952)	Boyd et al (1954)	Walter & Price (1955)	Walter & Price (1955)	Miyaji et al (1955)	Frkovich et al (1956)	Nicholson et al (1957)	Present series	Ochsner et al (1952)	Miyaji et al (1955)	Nicholson et al (1957)	Present series
Number of cases	331	301	207	159	406	252	910	174	-	-	-	20
Type of series	R	G	R	N	G	R	G	G	R	G	G	G
	B S	B S	B S	B S	B S	B S	B S	B S	F O	F O	F O	F O
Squamous	49.5	45.2	60.4	20.1	34	52	56	52.3	19	22.2	32	25
Undifferentiated under various descriptions	30.5	40	23.6	47.8	34	31	37	31.6	30	31.1	58	30
Adenocarcinoma	19.9	14.3	15.5	28.3	32	16	6	12.7	51	46.7	8	30
Bronchiolar carcinoma		0.5				1		2.3				10
Others			0.5				1.1	1.1				5
Unknown				3.8								

Figures are Percentages

R = Resection N = Necropsy G = General

B S = Both Sexes F O = Females Only

TABLE 13.

SITE OF GROWTH IN BRONCHIAL TREE. PRESENT SERIES AND OTHERS.

Author.	Oehsner et al (1952)	Aufses (1953)	Boyd et al (1954)	Victor (1955)	Nicholson et al (1957)	Present series	Gray (1948)
Number of cases.	948	959	403	4151	910	280	
	%	%	%	%	%	%	Relative weight of right and left lung.
R.M.B.		9	4.5			7.9	
R.U.L.		25	23		22.5	24.3	
R.M.L.		2	3		3	2.9	
R.L.L.		18	10		19	18.6	
Unknown		5					
Hilum			12				
Combined			2.5				
L.M.B.		6	3.2			6.4	
L.U.L.		17	15		25.5	24.6	
L.L.L.		12	8.7		15	15.3	
Unknown		6					
Hilum			12.6				
Combined			0.5				
Right lung.	53	59	55	53.2	51	53.7	53.3
Left lung.	47	41	40	45.5	49	46.3	46.7
Carina.			2				
Unknown			3				
Bilateral				1.2			

TABLE 14.

HISTOLOGICAL TYPE BY SITE OF GROWTH.

	Site.								
	* RMB.	RUL.	RML.	RLL.	LMB.	LUL.	LLL.	Site unknown.	Total
No. in whole series.	22	68	8	52	18	69	43	11	291
No. with known histology.	19	32	7	37	10	33	31	5	174
Squamous.	8	13	5	17	7	21	20	-	91
Undifferentiated.	9	14	1	10	2	8	8	3	55
Adenocarcinoma.	2	4	1	7	-	4	3	1	22
Bronchiolar carcinoma.	-	1	-	2	-	-	-	1	4
Malignant adenoma.	-	-	-	1	1	-	-	-	2

* Abbreviations as given in text, page 48.

TABLE 15.

HISTOLOGICAL TYPE BY AGE.

Histological Type.	Sex	Age Group											Total	% *
		<35	-39	-44	-49	-54	-59	-64	-69	-74	-79	-84		
Squamous	M	2	1	2	6	14	20	22	13	5	1	-	86	56.0
	F	-	-	1	2	-	-	-	2	-	-	-	5	25.0
	Total	2	1	3	8	14	20	22	15	5	1	-	91	52.3
Undifferentiated.	M	2	1	2	5	8	9	11	7	3	1	-	49	31.8
	F	1	-	1	-	1	1	1	-	-	1	-	6	30
	Total	3	1	3	5	9	10	12	7	3	2	-	55	31.6
Adenocarcinoma.	M	-	-	-	1	3	4	2	2	3	1	-	16	10.4
	F	-	1	1	-	-	-	2	-	-	2	-	6	30.0
	Total	-	1	1	1	3	4	4	2	3	3	-	22	12.7
Bronchiolar Carcinoma	M	-	-	-	-	-	-	1	-	-	-	1	2	1.3
	F	-	-	1	-	-	-	-	-	1	-	-	2	10.0
	Total	-	-	1	-	-	-	1	-	1	-	1	4	2.3
Malignant Adenoma.	M	-	-	-	-	-	-	-	-	1	-	-	1	0.6
	F	-	1	-	-	-	-	-	-	-	-	-	1	5.0
	Total	-	1	-	-	-	-	-	-	1	-	-	2	1.1

* Totals for Males and Females are expressed as percentages of growths occurring in each sex separately.

Totals for both sexes combined are expressed as percentages of all growths.

TABLE 16.

DISTRIBUTION OF MAJOR HISTOLOGICAL TYPES BETWEEN MAIN AND OTHER BRONCHI.

	Site.			
	Main bronchi.		Others.	
	No.	%	No.	%
Squamous.	15	53.6	76	56
Undifferentiated.	11	39.4	41	30
Adenocarcinoma.	2	7	19	14
Total.	28	100	136	100

TABLE 17.

INCIDENCE OF METASTASES. PRESENT AND OTHER SERIES.

Histological type.	No. of Cases.	Mediastinal glands.	Spleen.	Bone Marrow.	Liver.	Kidney.	Supra-renal glands.	Thyroid.	Brain.	Bones.	Pancreas.	Skin.	Other lymph glands.
Squamous.	18	66.6	-	10	27.8	5.5	33.3	-	23	5.5	-	-	5.5
Undifferentiated.	33	60.5	15.1	32	51.5	15.2	30.4	15.2	48	15.2	21.2	6	15.2
Adenocarcinoma.	12	75	8.3	28.5	41.6	8.3	50	8.3	22.2	16.6	8.3	-	25
Bronchiolar Ca.	4	-	-	-	-	-	-	-	-	-	-	-	50
Malignant adenoma.	1	-	-	100	100	-	-	-	-	-	-	-	
Total	68	60	8.8	22.7	40	10.3	32.4	8.8	32	11.7	11.7	2.9	13.2
Other Series.													
Ochsner and Debakey (1942)	2579	75 *			34.4	16	17.6		14.6	20.4			
Miyaji et al (1955).	300	94 x			38	28	29		19	22			

* Represents figure for "regional lymph gland".
x Represents figure for "lymph nodes".

Chapter IV.

C A S E F I N D I N G

Hospital organisation throughout the survey period. Criteria of diagnosis. Methods of case finding; mass miniature radiography. Time spent in diagnosis.
Tables 18 - 24.

Hospital Organisation Throughout the Survey Period.

During the first eighteen months covered by this survey, Bedford General Hospital comprised two separate establishments each with its own medical records. No Nosological Index was kept and the filing of records was quite inadequate by present day standards. With the introduction of the National Health Service the two hospitals were joined administratively and an effective Nosological Index was started in 1951 coming into

full operation in 1952. Cases from earlier years have been added to the Index if still alive in 1951 but this applied to relatively few cases of lung cancer. There was, thus,little information available at the time prior to 1951 of how many patients with lung cancer, or any other illness, were being seen each year. This lack of information is one reason why few cases are found in the early years of this survey. There were two tuberculosis dispensaries in the area which in 1947 were combined in the form of a new chest clinic situated in the grounds of one wing of the General Hospital. This, with its closer ties with thoracic surgical centres which were themselves expanding with the appointment of a part-time thoracic surgeon to the hospital in 1952, offered increased diagnostic and therapeutic services to the practitioners of the area. A greatly improved pathological service was provided from 1950 which increased the accuracy of diagnosis by enabling bronchoscopies to be carried out in the hospital, by the introduction of exfoliative cytology and by an increase in the number of post-mortem examinations. No static Mass Miniature Radiography (M.M.R.) vans have been sited in the area though visits were paid by an M.M.R. unit every two or three years. A 70 mm. (Odelca) camera was installed in the chest clinic in 1953 enabling a weekly session to be organised for the use of general practitioners who have employed to an increasing degree this means of a quick radiographic check on their patients. Thus, facilities for diagnosis and treatment have improved over the past ten years together with better record keeping and the effect is

reflected in the increase in the number of cases diagnosed and treated at the hospital during the period of the survey. This annual increase was marked up to 1950 since when the rate has become slower.

Criteria of Diagnosis.

The necessity for proof of diagnosis when assessing a series of cases is obvious and in dealing with bronchial carcinoma the only definite proof that is acceptable is histological examination of the primary growth or of a secondary deposit where the histology definitely indicates a lung primary. Such proof was obtained in 193 patients in this series, 66.5% of the total, as shown in Table 18. The remaining 98 cases were accepted on good clinical grounds, radiographic appearances consistent with bronchial carcinoma and the subsequent death of the patients concerned. Of these 98 patients, 28 had good bronchoscopic evidence of growth but biopsy was impossible or negative. The finding of neoplastic cells in the sputum or pleural fluid or bronchial washings has not been considered as histological proof, as the reliability of this investigation was to be assessed and therefore prior assumption of its reliability could not be made. In fact, 24 of these 98 patients had malignant cells found in their sputum or pleural fluid and if this were accepted as histological proof it would bring the total of proven cases up to 217, 74.6% of the total. The reason in the majority of clinically diagnosed patients for not obtaining

histological proof was that the patient when seen at hospital was too ill for procedures such as bronchoscopy or thoracotomy. In a few cases investigation was refused and in several, although the patient's general condition was fairly good, his age precluded any attempt at resection, although this factor has been decreasing as surgical and anaesthetic techniques have improved. In recent years the utmost endeavour, within reason, has been made to confirm a diagnosis of suspected lung cancer, for even if the tumour is inoperable radiotherapy may be employed and, at worst, some prognosis can be offered to the patient's relatives.

Methods of Case Finding.

The number of cases diagnosed in the various hospital departments is shown in Table 19. The majority, 214 out of 291, were seen at the chest clinic. Of these 176 were referred for consultation because of the presence of symptoms, 22 were referred to the miniature (70 mm.) film session and 8 cases were referred to the chest clinic for further investigation from the M.M.R. Unit operating in the county. Eight patients were found to develop bronchial carcinoma when they were under observation or treatment by the staff of the chest clinic for other conditions, 1 for chronic bronchitis and emphysema, 1 for a spontaneous pneumothorax and 6 for pulmonary tuberculosis, 3 active and 3 inactive. Seventy seven cases were referred to other departments in the hospital, nearly all to the physicians' wards of out-patient sessions, a few being referred to the surgical staff because of palpably enlarged lymph glands.

One was sent to the Ear, Nose and Throat Department complaining of hoarseness and one was picked up on routine radiography when attending an ante-natal clinic. Of these 77 cases, 54 were referred to the chest physician for opinion or interest, thus enabling the clinic staff to keep records of 92% of all the lung cancers referred to the hospital.

It can be seen from Table 19 that the number of cases picked up by M.M.R. is very small, only 2.7% of the series. This is due to the infrequent visits paid by the units to this area. The pick-up rate during 1954, 1955 and 1956 for the region covered by the St. Albans M.M.R. service, which includes this area, was 11.3, 9.2 and 6.3 cases per 100,000 persons examined (Table 20). Table 21 shows the pick-up rates of various M.M.R. surveys carried out in Europe and the U.S.A. in recent years. Excluding the high figure of Brett et al (1956), the average yield is 9.5 cases of lung cancer per 100,000 persons examined, so the success of this case finding method is about average in this area. The use of M.M.R. surveys will be discussed later.

Only 22 cases, 7.6% of the total series, were picked up through the 70 mm. minifilm clinic but this has only been functioning since 1953 and during the last two years of the survey 20% of the 85 cases diagnosed were picked up by this means. Table 22 shows the pick-up rate over the past three years with an average of 414 cases of lung cancer per 100,000 persons.

Mass Miniature Radiography.

The use of mass radiography has been applied primarily to the search for persons with pulmonary tuberculosis. These tuberculosis case-finding surveys have had, almost as a sideline, the discovery of other unsuspected pulmonary disease and the results of several surveys, mainly in the U.S.A., have been publishedwith details of the number of lung cancers picked up. Table 21 sets out the more important of these and it can be seen that the number of cancer cases per 100,000 persons radiographed varies considerably. The major factor in this variability is the selection of population for the survey, rates varying from 2 to 12 cases per 100,000 persons examined are usual. When younger persons are excluded from the survey or the analyses, the rates are higher. Overall figures for Great Britain cannot be obtained from the Ministry of Health as the Chief Medical Officer's annual report fails to differentiate lung cancer from other intra-thoracic neoplasms in the review of mass radiograph findings. Opinions vary as to the use of mass radiography campaigns for this purpose. In theory, it should be very successful as early asymptomatic cases should be picked up and a high cure rate obtained. In practise, however, there are many difficulties. Persons who volunteer for mass radiography are usually young and in some surveys up to two thirds of persons were under 40 years of age and up to two thirds were women. For example in the Philadelphia survey, the following rates were obtained :- 37 per 100,000 for whole

series, 3 per 100,000 for females, 69 per 100,000 for males and 284 per 100,000 for males over 45 years of age. In the Los Angeles survey the figures were 11.4 per 100,000 in the whole series, 33 per 100,000 for persons over 45 years and 55 per 100,000 for males over 45 years. Unselective radiography thus appears to involve a considerable waste of time, money and skill. The interpretation of miniature films can be difficult and up to 50% of cases missed thereby (Garland, 1955). Failure to follow up suspect films can also lose a number of cancer cases (Gowen and Frank, 1952; Sherman, 1956).

The number of M.M.R. cases in this series is too small to analyse in detail. Not all cases picked up by this method are asymptomatic, over a third in this series had symptoms but as will be shown later, the resectability rate of "survey-detected" cancers is, on the whole, higher than that of cases referred to hospital because of definite pulmonary symptoms.

It is evident that the detection of early lung cancer can be achieved by mass radiographic methods and that such cases are frequently operable and have therefore in the present state of knowledge, a better chance of cure than those cases diagnosed after the onset of symptoms. Such mass surveys must be selective if they are designed specifically to find lung cancer cases. An enormous number of films would be required annually to cover even the most susceptible group, i.e. men over 45 years, in a nation-wide survey. It has been stated that even annual films of such persons will miss an appreciable number of growths and more frequent

films have been advocated by Churchill, by Ochsner and by Blades (Garland, 1955). In the Los Angeles survey, however, which entailed annual films over several years only 11% of all lung cancers found by any means in the population surveyed were missed by filming, showing that an annual film does detect the majority of cases. Making such films compulsory, at whatever time interval, appears a most unlikely event in Great Britain at the present time.

Siegal, Plunkett and Locke (1955) reported on the findings of those hospitals in New York State which took admission films of all patients. These findings were based on 254,549 patients over 15 years of age and they refer to the pick-up rate of "tumour suspects" per 1,000 patients. The rates per 1,000 were men 8.2, women 2.5 and total 4.4. When persons over the age of 45 only were considered, the rate for men was 13.6 and for women 6.9. About 10% of these were found, on investigation, to have lung cancer. No indication is given of how many patients were picked up who would not have been without the routine admission film but it seems to confirm the advantages of filming men over 45 years of age for this purpose. Thus, miniature radiography applied to specific groups of persons has been shown to be more successful than when applied to the general public and this may well be a fruitful method of case finding in the future, particularly if the search for tuberculous cases is gradually shifted from the younger to the older age groups.

Time Spent In Diagnosis.

It is axiomatic that the earlier a tumour can be diagnosed, the greater is the chance of surgical removal. The tragedy of lung cancer lies mainly in the fact that by the time it produces sufficient symptoms or signs to cause the patient to attend hospital the tumour is frequently inoperable. The time spent in diagnosis can thus be divided into the period of symptoms before the patient seeks the advice of his practitioner, the period during which he is treated symptomatically, often for bronchitis or fibrositis, the time spent after his being referred to hospital before a diagnosis is made and the patient transferred to the charge of a thoracic surgeon, and the final period before operation is performed.

In this series, a date of onset of symptoms has been estimated in each patient, the accuracy depending on the type of symptoms, haemoptysis being relatively easy while gradually increasing dyspnoea or lassitude very difficult to date back to its commencement. No information is available on the time each patient was treated by his practitioner before being referred to hospital as it was felt inadvisable to ask patients this question. The date of diagnosis in each case has been taken as (a) the first occasion on which histological proof of the diagnosis was obtained or (b) in those cases without such proof, when the definite diagnosis was entered in case notes or transmitted to the patient's practitioner. In those cases in whom histological proof was obtained a date of diagnosis

has in some instances been delayed by the time required to arrange bronchoscopy. This might take up to 10 days and confirmation of a provisional diagnosis might be delayed for that time. The date of treatment has been taken as the date when a patient underwent resectional surgery or commenced a course of radical radiotherapy.

A. Interval from onset of symptoms to hospital attendance.

Table 23 sets out this interval for each year of the survey, as an average for all patients in each year. It can be seen that there has been little change over the years, the average being 18.5 weeks. This compares with figures of 28.2 weeks reported from Manchester, 1948 to 1954, by Nicholson et al (1957), and 11.3 weeks reported by Thompson (1957). Before being referred to hospital 47% of the patients had symptoms for less than four months but 8.9% had symptoms for over a year. Table 19 shows the duration of symptoms of the patients picked up by different methods. They follow the methods as expected, the shortest period of symptoms, 9.7 weeks, being among those picked up by M.M.R., next, 14 weeks, by those with slight symptoms referred to the practitioners minifilm clinic. Then follow those under observation for other diseases, 18.8 weeks, and then patients referred for consultation because of definite pulmonary symptoms, 18.9 weeks. The most long lasting symptoms, averaging 20.9 weeks, were among the patients referred to physicians and surgeons, usually with advanced disease.

B. Interval from hospital attendance to diagnosis.

Table 23 shows this period for each yeaf of the survey.

Unlike the duration of symptoms, this has decreased significantly over the past ten years. This, however, is liable to misinterpretation. Further reference to Table 19, shows the interesting fact that speed in diagnosis has varied almost inversely with duration of symptoms. General physicians and surgeons have made the swiftest diagnoses, frequently their patients presenting with evidence of secondary spread, then symptomatic cases referred to the chest clinic, then the minifilm clinic patients and next those picked up by M.M.R.. Finally the longest delay in diagnosis was in those cases in whom attention is misdirected at known pre-existing pulmonary disease, this confirming the fact that cancer arising in such patients is liable to be misdiagnosed for some considerable time unless there is constant awareness of the possibility of its occurrence.

Thus a drop in the interval to diagnosis might mean that a higher proportion of easily diagnosed cases, a term unfortunately synonymous with advanced, were seen in the later years but this is, in fact, not so as the proportion of resections has not been falling as it would have done if more advanced cases had been seen. The overall average interval for diagnosis was 5.6 weeks. In the five year period 1947 - 1951 it was 8.3 weeks and from 1952 - 1956 it was 4.2 weeks and this reflects the benefits of an increase in facilities, more modern diagnostic measures and greater "physician awareness" of the condition. Table 24 sets out the interval for diagnosis in another form and shows that 83.6%

of the cases were diagnosed within two months but a small proportion, 7.1%, took over six months and their chance of effective treatment thereby reduced. In the final year of the survey 93% of cases were diagnosed within two months. In a report on the last 75 consecutive cases of lung cancer seen at the Worcester Chest Clinic, Moyes (1957) stated that 90.7% of his cases were diagnosed within two months. Thompson (1957) has criticised the delay occurring in chest clinics before referring these patients to a surgeon. The figure he quoted was 3.8 months (16.4 weeks). In this area patients were referred to a surgeon for opinion immediately on diagnosis and the comparable figure of 5.6 weeks points to a certain variation from one area to another. Similarly, the resection cases in Moyes' series were diagnosed, and then presumably referred to a surgeon, in an average of 2.6 weeks.

A + B. Interval from onset of symptoms to diagnosis.

This combined interval has dropped fairly steadily over the years with an overall average of 24.1 weeks. Published figures for this interval have varied from 15.2 weeks to 43.3 weeks (Lindskog, 1946; Overholt and Schmidt, 1949; Taylor and Waterhouse, 1950; Bignall, 1955; Oswald, 1956).

C. Interval from diagnosis to treatment.

The average period was 2.8 weeks, a figure not likely to be improved very much as this includes transfer to a surgical unit and time for any additional investigation considered necessary.

A + B + C. Interval from onset of symptoms to treatment.

This overall interval is on an average for the resection

cases, 26.9 weeks (18.5 + 5.6 + 2.8). This compares with such figures as 39 and 26 weeks for patients in 1940 and 1950 respectively (Sellors, 1955), 34.7 (Smiley and Cheesman, 1956) and 32 (Thompson, 1957).

The figures thus show that the diagnostic services of this hospital are comparable with most of those in other published reports and better than some. It is evident that miniature radiography, particularly of selected population groups can pick up many early cases and that this method of case finding is the best method of detecting early cases of lung cancer. The question of whether these mainly asymptomatic patients are more amenable to surgery than symptomatic patients will be discussed in a later section.

TABLE 18.

MEANS WHEREBY HISTOLOGICAL PROOF OF DIAGNOSIS WAS OBTAINED.

Bronchoscopy	102
Subsequent operation	19
Thoracoscopy	1
Biopsy of secondary deposit	14
Neoplastic tissue coughed up	1
Autopsy	56
Total	193

TABLE 19.

ANALYSIS OF PATIENTS REFERRED TO VARIOUS HOSPITAL DEPARTMENTS.

Department	Chest Clinic Consultations.	Chest Clinic 70 mm. film sessions.	Chest Clinic. Referred from M.R.U.	Chest Clinic. Patients under observation for other condn.	Other hospital departments.	Total.
No. of cases	176	22	8	8	77	291
% of total	60.6	7.6	2.7	2.7	26.4	100
No. of resectable cases	33	7	5	2	5	52
% resectability	18.7	31.8	62.5	25	6.5	17.9
1947	2					2
1948	12				1	13
1949	18				2	20
1950	24		3		5	32
1951	18			1	10	29
1952	24		3		12	39
1953	19	1		1	13	34
1954	20	4	1	1	11	37
1955	16	10	1	3	12	42
1956	23	7		2	11	43
Average duration of symptoms in weeks	18.9	14	9.7	18.8	20.9	18.5
Average period of diagnosis in weeks	4.4	5.7	8.5	26.3	3.7	5.6

TABLE 20

DETECTION OF LUNG CANCER CASES BY ST. ALBANS'S MASS RADIOGRAPHY UNIT.

Year	Total number radiographed	Number of cases detected	Rate per 100,000
1954	61,905	7	11.3
1955	64,763	6	9.2
1956	79,280	5	6.3
Total	205,948	18	8.7

TABLE 21

DETECTION OF LUNG CANCER CASES BY MASS RADIOGRAPHY. PUBLISHED SERIES.

Author	Place	Year	No. Surveyed.	No.of cases of lung cancer	Rate per 100,000	Resectable.
Gould (1945)	U.S.Public Health Service.	1944	442,252	9	2.3	
Bondi & Leites (1952)	New York.	1949	228,375	20	9	60%
Scamman (1951)	Boston.	1949/50	536,012	43	8	46%
Gowen & Frank (1952)	Illinois.	1949/50	156,724	10	6.3	
Boucot & Sokoloff (1955)	Philadelphia.	1949/52	142,156	52	37	30%
Greenberg (1956)	Connecticut.	1949/53	358,283	33	9.2	
Guiss (1955)	Los Angeles.	1950	1,867,201	213	11.4	40%
Korteweg (1953)	Amsterdam	1951/52	- *	-	2.4	
" "	Schiedam	"	-	-	14.3	
Brett et al (1956)	Islington	1952/54	87,261 (adults)	115	132	
Geddes (1957)	Glasgow	1957	714,906 *	180 +	25 +	

* = Over 14 years of age. + = Provisional figures.

TABLE 22

DETECTION OF LUNG CANCER CASES THROUGH 70 MM. FILM CLINIC.

Year	Total No. radiographed	No. of cases detected	Rate per 100,000
1953	x	1	x
1954	1603	4	248.8
1955	1719	10	581.7
1956	1750	7	400
Total	5072	22	414 *

x = figure not available * = excludes 1953

TABLE 23

AVERAGE DURATION OF SYMPTOMS AND TIME REQUIRED FOR DIAGNOSIS.

Year	Interval in weeks		
	Onset of symptoms to hospital attendance a	Hospital attendance to diagnosis b	Total a + b
1947	8.6	5.0	13.6
1948	18.5	10.9	29.4
1949	20.6	9.7	30.3
1950	11.6	9.6	21.2
1951	24.9	4.9	29.8
1952	21.9	2.4	24.3
1953	24.9	4.2	29.1
1954	16.3	7.3	23.6
1955	15.9	5.0	20.9
1956	17.6	2.6	20.2
Average	18.5	5.6	24.1

TABLE 24

TIME REQUIRED FOR DIAGNOSIS. PRESENT SERIES AND MOYES' SERIES.

Interval, hospital attendance to diagnosis, in weeks	Present series				Moyes' series
	Inoperable cases	Resection cases	Total	%	%
0 - 1	123	26	149	51.2	49.4
2	45	8	53	18.3	17.3
3	15	3	18	6.2	13.3
4 - 7	19	4	23	7.9	10.7
8 - 25	18	9	27	9.3	5.3
26 - 51	13	2	15	5.1	2.7
over 51	6		6	2.0	1.3

CHAPTER V

CLINICAL FEATURES IN DIAGNOSIS

Symptomatology. Physical signs; in the lungs, metastatic. Clinical features of particular interest; haemoptysis, wheeze, finger clubbing, hypertrophic pulmonary osteoarthropathy, superior vena caval obstruction, superior sulcus syndrome, neurological manifestations, thrombophlebitis migrans. Association between pulmonary tuberculosis and lung cancer. Tables 25 - 28.

References are made in this section to radiographic reproductions displayed in the APPENDIX. Plates 1 - 6.

Symptomatology.

The symptoms of which patients in this series complained when referred to Hospital are listed in Table 25. The

commonest are seen to be breathlessness on exertion, productive cough, haemoptysis, loss of weight, chest pain and tiredness. Certain symptoms, such as haemoptysis, could be attributed to the growth itself but the commonest symptoms, exertional dyspnoea and productive cough, are present in many persons who smoke cigarettes and are past middle age and it was usually impossible to determine to what extent those symptoms were due to chronic bronchitis and how much to the presence of a neoplasm. A dry irritating cough or one which had increased suddenly were much more suggestive symptoms. Symptoms could be divided into general and local groups and those due to metastatic deposits.

General. These are common to most malignant growths and include lassitude (present in 23.8% of patients when first seen at hospital), malaise and loss of appetite (7.2%), loss of weight (38.8%), fever (1.7%), night sweats and increasing emaciation.

Local. These are due directly to the presence of the growth itself. Cough was present in 73.2% and was dry when the result of bronchial irritation and productive when infection developed distal to a partial bronchial stenosis or when, as mentioned above, chronic bronchitis was present. Dyspnoea on exertion was present in 52.7% of cases. This was usually out of proportion to the amount of lung tissue replaced by neoplasm and more often the result of partial bronchial obstruction. Contributory factors were consolidation distal to the tumour, anaemia and pain on respiration. Haemoptysis (43.4%)

is a symptom so commonly associated in the public mind with lung cancer, it is analysed in more detail in the following section. Chest pain (29.6%) varied from a dull retrosternal ache to a localised pleuritic pain. Existing clinical records are inadequate to attempt an analysis of the causes of pain in lung cancer such as was described by Blanshard (1955). Recent respiratory infections (7.2%) were not uncommon as the symptom which brought patients to hospital consultation, particularly in the recent years of the survey when slowly resolving pneumonias have been regarded with suspicion by an increasing number of general practitioners. Wheezing (3.1%) was usually a late symptom and occurred in cases where either growth or enlarged glands caused compression of the major bronchi. The significance of wheeze as a sign will be discussed later. Hoarseness (3.8%) was also in most cases a late symptom. In five of the eleven cases concerned, vocal cord paralysis was proved, in the other six it was probably present but laryngoscopy was not carried out as the condition of the patient was too poor in each case to warrant it. In only two out of the eleven cases was the growth situated in the lower lobes and hilar shadow enlargement or a broadened mediastinum was seen on radiography in each case.

Metastatic. These are the results of secondary spread, either intrathoracic causing symptoms of superior vena caval obstruction and dysphagia, or extrathoracic from lymphatic or haematogenous dissemination. A minority of patients had these symptoms when referred to hospital but when present the

prognosis was usually very poor. The commonest group of extrathoracic symptoms was that due to involvement of the nervous system. Of the whole series, twelve (4.1%) presented at hospital with a variety of cerebral symptoms. Defects in memory or speech, symptoms of raised intracranial pressure, focal pareses or paralyses and even dementia were included.

A comparison of the frequency of the commonest symptoms reported in five series is given in Table 26. The figures of Brooks et al (1951) differ considerably from the others due to the fact that it was a highly selected series.

Physical Signs.

In the Lungs.

The physical examination of a patient with an early carcinoma of the lung may reveal no abnormality whatever. In 117 patients no abnormal signs in the lungs were detected and as this represents over a third of the series it indicates clearly how misleading can be a chest which looks and sounds normal. The commonest abnormal signs at the first hospital visit were associated with pulmonary consolidation and/or collapse of varying degree or replacement of the lung by tumour mass. These were present in 120 patients and included alteration in the movement of the thoracic cage, position of the trachea and apex beat, change in percussion note, breath sounds, tactile and vocal fremitus. A localised wheeze,

produced by partial endobronchial obstruction, was present in 24 patients. The signs of a pleural effusion were noted in 20 patients. Chronic bronchitis with its attendant wheezing and crepitations was marked in 5 cases but was present to a lesser extent in many others, an expected finding in view of the age and smoking habits of the majority of the patients. A friction rub caused by acute pleurisy was heard in 3 cases, pulmonary oedema in 1 and signs of a pneumothorax in 1.

Metastatic.

Inside the thorax these are produced by secondary involvement of structures such as the pleura, the pericardium, lymph nodes, nerves and the chest wall. The physical signs varied with the extent of spread and on the patients' first hospital visit included pleural effusions in 32 cases, cardiac arrythmias in 3, superior vena caval obstruction in 13, vocal cord paralysis in 4 and diaphragmatic paralysis in 7 cases.

When extra-thoracic extension had occurred there were a variety of signs produced depending on the organs involved. These included enlarged lymph nodes in various sites usually supraclavicular or axillary, enlargement of the liver, nodules in the skin, pathological fractures and neurological abnormalities of considerable variability.

<u>Clinical Features of Particular Interest.</u>

Haemoptysis.

This occurred in 126 patients, 43.4% of the series. The

detailed analysis of those patients with haemoptysis is shown in Table 27. It was present in over half the men but in only one fifth of the women. There was no relationship to urban/rural distribution, presence of finger clubbing, smoking history or the site of the tumour. It occurred more often in patients over 60 years old and patients with haemoptyses tended to have a shorter history before coming to hospital as would be expected. Positive evidence of growth was obtained on bronchoscopy more often in patients with haemoptysis although the site of tumour was unrelated. With regard to histology, the proportion of squamous growths in the haemoptysis group was higher than in the non-haemoptysis group whereas the proportions of undifferentiated growths and adenocarcinomata were much lower. It occurred in 3 out of 4 bronchiolar carcinomata but surprisingly in neither of the malignant adenomata.

A slight difference is evident in the resectability. Only 15.1% of the haemoptysis group underwent resection whereas 20% of the non-haemoptysis group did so; 17.9% of the whole series underwent resection. Thus, although haemoptysis occurs more often in squamous growths than in the more malignant histological types and it tends to bring the sufferer to hospital more quickly than patients who do not have it, the causative neoplasms are not more amenable to surgery and its apparently useful alarming nature as a symptom is lost by the poor resectability of the tumours which cause it.

The cause of haemoptysis varies. Bronchial artery erosion is one cause. Although haemorrhage from a major vessel is uncommon as the pulmonary vessels in the vicinity of a growth

are frequently thrombosed, the bronchial arteries undergo proliferative changes and as long ago as 1938 Wood and Miller suggested that haemoptysis was often due to damage to bronchial arteries. Some confirmation of this was obtained by Cudkowicz and Armstrong (1953) who found, when examining primary bronchial carcinomata histologically after dye injection of the bronchial circulation, that the tumour contained thin walled lacunae which were in communication with the bronchial arteries which, in life, would maintain a considerably higher blood pressure than the pulmonary circulation.

Wheeze.

Those patients in whom wheezing had been a feature of chronic bronchitis for years before a carcinoma of the lung became apparent are not being considered. Nine patients complained of a newly developed wheeze but on examination it was found to be present in 24 patients altogether. In some cases it was present on inspiration, in some on expiration but usually in both phases. It could be heard over both lungs in a few cases but in the majority was confined to the affected lung and in 15 cases best heard close to the sternum in the fourth intercostal space. No effect of posture was recorded. Each of the 24 patients had either a tumour in a major bronchus or a more peripheral tumour associated with a mass of hilar glands.

Finger Clubbing.

This sign was present in 86 patients in the series, an

incidence of 29.7%. It varied in degree from thickening of the nail bed to the "drumstick" appearance of fingers and toes. Table 28 sets out a comparative analysis of those patients with and without finger clubbing. It occurred in 32.4% of men but in only 8.8% of women; it was commoner in patients over the age of 60 than under and in patients with histories of more than three months duration rather than under three months. The histological type of growth had no clear cut connection though a higher proportion of adenocarcinomata occurred in patients with clubbing than in those without it. This is probably related to the fact that 22% of patients with clubbing had peripheral growths compared with 13.7% of patients without it. It was unrelated to the lobe in which the growth was situated except for an unexplainable and notable infrequency of clubbing with left lower lobe growths. Its presence had little relation to the treatment, resection being carried out in 15.1% of patients with clubbed fingers and in 19.0% of those without, and radiotherapy in 16.3% and 17.0% of such cases respectively. Cudkowicz and Wraith (1957) investigated 27 cases with clubbed fingers and confirmed the opinion expressed by others, that no common factor could be found. They considered an additional anomaly was present, probably the formation of precapillary bronchopulmonary anastamoses in abnormal pulmonary lobes. Cudkowicz and Armstrong (1953) had found that in two cases of lung cancer associated with finger clubbing there was thrombosis and recanalization of pulmonary artery branches by the vasa vasorum of the bronchial circulation. Hippocrates

noticed the presence of clubbed fingers in the 5th century, B.C.. His description, "The finger nails are bent and the fingers grow hot, especially at the tips....." was applied to persons with empyema not bronchial carcinoma but no satisfactory explanation of the phenomenon has been elicited in the past two thousand years.

Hypertrophic Pulmonary Osteoarthropathy.

This interesting condition was first described in detail by Marie (1890) and consists of an ossifying periostitis of the distal portions of the bones of the forearm and leg with an associated synovitis and frequently accompanied by clubbing of the extremities. It has been reported uncommonly in association with various non-pulmonary diseases (Semple and McCluskie, 1955) but is nearly always caused by pulmonary disease, usually bronchial carcinoma, bronchiectasis or chronic lung abscess. Price-Thomas and Drew (1953) stated that no condition is associated with osteoarthropathy so constantly as fibroma of the visceral pleura. In view of its connection with some non-pulmonary conditions the term, "Generalised hypertrophic osteoarthropathy" has been suggested by Gall, Bennett and Bauer (1951) as being more accurate.

Semple and McCluskie estimated the incidence at 1 to 2% of lung cancer cases, Jack (1952) found it in only 0.4% of his series while Ray and Fisher (1953) quoted the incidence as 10% among their 139 patients. Ellman (1953) found 3% among 200 similar patients while Simpson (1956)

in a brief review of the subject stated that the incidence has been quoted as high as 50%. One reason for the variability in these reports is the inclusion by some authors of finger clubbing as the first stage of osteoarthropathy, an inclusion which is unjustifiable according to Semple and McCluskie who stated that clubbing was a very variable feature in the 24 patients with arthropathy whom they studied.

In this Bedfordshire series, five patients suffered from this condition, an incidence of 2%. Four had definite finger clubbing and the other had no or very slight clubbing. The symptoms of arthropathy are occasionally the presenting feature in cases of lung cancer, as in 6 cases of Pattison, Beck and Miller (1951) and 16 out of the 24 reported by Semple and McCluskie. In two Bedfordshire cases arthropathy developed after other significant pulmonary symptoms but in the other three it had been present for over nine months before pulmonary symptoms developed.

The condition is said to occur in patients with slowly growing tumours nearly always peripheral and with central necrosis, but not with oat cell growths (Semple and McCluskie). Thirteen of the 14 cases reported by Ray and Fisher accompanied peripheral growths and they quoted several authors who have found the same association.

Three cases in the present series definitely had peripheral growths while the other two had probably started peripherally but as both were well advanced when the patients presented the exact site was difficult to determine. The

histological type was not identified in two of the cases but the growth in the other three consisted of one squamous, one undifferentiated and one adenocarcinoma.

Various theories as to aetiology have been propounded, toxic absorption from the tumour (Craig, 1937), arterial hypoxia (Van Hazel, 1939) and a neural reflex, being a few examples. Denervation of the lung hilum can cause regression of the condition (Brea, 1948; Flavell, 1956) and this supports the possibility of a neural reflex but it must be remembered that the lungs are bilaterally innervated from the vagi and the effect of division might depend on resultant alteration in the intrapulmonary vascular network. This theory is supported by Vogl, Blumenfeld and Gutner (1955). The work of Cudkowicz and Armstrong referred to in a previous section forms the basis of a possible explanation of the apparently unrelated clinical features of this condition.

Superior Vena Caval Obstruction.

This condition, caused by the extension of malignant growth to involve the mediastinum first by lymphatic spread and finally in many cases by invasion of the mediastinal tissues themselves, is universally recognised as being of grave import.

Any space filling lesion in the superior mediastinum may cause it but secondarily involved lymphatic glands are responsible for most cases and like pulmonary osteoarthropathy, although there are other causes, bronchial carcinoma is by far

the commonest. Four out of every 5 cases of this syndrome according to Szur and Bromley (1956), are due to lung cancer.

It was present in 25 patients in the present series, 8.6% of the total. In 13 cases it was present when the patient was referred to hospital and in 12 cases it developed later. Of the 13 cases only 3 complained of a choking sensation and 4 of swelling of the face and neck, but in the other 6, raised jugular venous pressure was noted and in several cases an unpleasant tight sensation could be induced by the patient leaning well forward.

It occurred in 23 men and 2 women which is the expected sex distribution. None of those presenting with an established vena caval obstruction had symptoms for less than one month. The distribution of the growth in 23 cases where known was as follows : RMB 4, RUL 9, RML none, RLL 3, LMB 1, LUL 4 and LLL 2.

There was thus a preponderence of growths in the right lung compared with the left, and in the upper lobe compared with the lower due to an unusually large number of growths in the right upper lobe. The tumour type was ascertained in only 8 cases; squamous in 3 cases and undifferentiated in 5. In the series of Szur and Bromley the same preponderence of right sided growths and undifferentiated growths was noted. They also commented that bronchoscopy in such cases was often difficult or impossible.

Superior Sulcus Syndrome.

The typical features reported by Pancoast (1932) can be

produced by a variety of space-filling lesions, the commonest of which is a bronchial carcinoma situated at the apex of the lung. The local effects typical of such a tumour are erosion of the upper ribs, involvement of varying portions of the brachial plexus with resultant neurological effects in the arm and shoulder, and involvement of the sympathetic chain producing Horner's syndrome. To these specific abnormalities are added, of course, those that could be produced by a malignant growth whatever its situation. Not all the characteristic abnormalities are present in every case but the presence of at least two of the three characteristic local effects in a patient who has an apical neoplasm is generally considered sufficient to apply the term "Superior sulcus syndrome".

Three such cases occurred in this series. Each was caused by a squamous carcinoma situated in the upper zone, though not initially at the extreme apex of the lung, the right side in two cases and the left in one case. In only one was the full clinical picture evident with rib erosion and brachial and sympathetic nerve involvement, the case being fully described (Young, 1954) owing to its longevity of eight and a half years before the growth spread and initiated the superior sulcus syndrome (Plates 1 and 2). In each of the other two patients the brachial plexus was involved causing weakness and pain in the affected arm, erosion of the ribs was present causing chest pain, but Horner's syndrome was absent in both patients.

In one patient extensive active tuberculosis was

present, particularly in the area subsequently involved by growth (Plates 3 and 4), and in another minimal inactive tuberculosis was present. In these two patients it was chest and arm pain which gave rise to suspicion of malignancy.

Neurological Manifestations.

The effects that a bronchial carcinoma can produce on the nervous system can be divided into four main groups :-

Cerebral metastases.

These were among the presenting features in 12 patients in this series. Four patients had squamous growths, 4 had undifferentiated growths, 2 had adenocarcinomata and in 2 cases the histological type was not ascertained. In 5 cases, the cerebral symptoms were present before local chest symptoms developed. The abnormalities produced by the cerebral secondaries were dementia in 1 case, focal fits in 4, loss of memory in 1, cerebellar ataxia in 1, hemiplegia in 4 and localised motor and sensory changes in 1. Personality change was not noted in any patient but can occur with a secondary deposit in the frontal lobe. Brain (1957) reported that 16 to 20% of cerebral secondaries were single deposits and operation to remove them might be justifiable after full investigation. No case in this series had such a deposit excised.

Spinal cord involvement.

It is uncommon to find secondary deposits in the spinal cord at autopsy but direct compression and damage to the cord can result either from direct extension of the growth or from

metastases in the vertebrae. The former was seen in 2 cases in this series, in one man of 27 years a complete paraplegia resulted from an undifferentiated tumour and in another man from a squamous superior sulcus tumour. Vertebral metastases with consequent cord damage were proved in one other case.

Peripheral nerve involvement.

The phrenic nerve may be involved in primary or secondary growth. Abnormal diaphragmatic movement was noted in 43 out of 120 patients screened. This was due in the majority to phrenic nerve damage though diaphragmatic fixation in one case at least was probably caused by a previous pleural effusion. The recurrent laryngeal nerves may be involved in a similar manner and 11 patients had hoarseness as one of their presenting symptoms. The brachial plexus is also liable to damage by a superior sulcus tumour as occurred in 3 patients. Other peripheral nerves can be involved by pressure from glandular masses. The intercostal nerves are sometimes involved by extension of the growth into the chest wall. Although it has been suggested that herpes zoster may be related in some cases to spinal cord or intercostal nerve involvement no proof has yet been forthcoming.

Carcinomatous neuromyopathies.

These consist of variable motor and sensory abnormalities usually affecting the limbs. Denny Brown (1948) was among the early authors to describe this condition, and unexplained peripheral neuritis was reported in 1.7% of the series of Lennox and Prichard (1950) and 2.2% in that of Lea (1952).

The cause may be Vitamin B deficiency (Hart, 1954) and this deficiency may also cause other uncommon neurological abnormalities which occur without obvious secondary neoplastic deposits such as subacute cerebellar degeneration, pyramidal tract involvement (McCaughey and Millar, 1955) and confusional psychoses (Cheraton and Brierley, 1957).

Thrombophlebitis Migrans.

This condition was first described in association with visceral cancer by Trousseau in 1877. Since then it has become recognised as one of the possible effects of such a cancer. The majority of such cases result from cancer of the pancreas but a bronchial carcinoma can cause it and Williams (1954) reported that at least thirteen such cases have been published and added four of his own. As the thrombophlebitis persists in spite of almost dangerously low prothrombin times resulting from the use of anticoagulants, it may be presumed that a clotting tendency is not the main factor involved. Tumour emboli are considered the most likely cause and these embolic cells may be arrested and form a nidus for clot formation. If they continue living a true secondary deposit can be seen microscopically.

No case with a definite thrombophlebitis migrans occurred in this series.

The Association Between Pulmonary Tuberculosis and Bronchial Carcinoma.

In this series there was evidence of concomitant pulmonary

tuberculosis in 18 cases, 6.2% of the total. The evidence was either radiographic, bacteriological or both. In 1 case tubercle bacilli were growth from sputum on one occasion only and in another case on two occasions only. Neither had any radiographic evidence of tuberculosis and it has been assumed that the source was either a minimal pulmonary focus, or more likely, an old infected hilar gland which had been broken up by neoplastic involvement thus liberating dormant bacilli. In 9 cases pulmonary tuberculosis was present though inactive at the time when the growth became obvious. In 5 of these the growth was situated near the obvious tuberculous foci and in the other 4 the sites of the two conditions were well separated but the presence of more closely associated minute tuberculous foci cannot be excluded. In 3 cases there was definite evidence of tuberculosis of the fibrocaseous type, in 2 of whom the growth was closely associated with the diseased area (Plates 3 and 4). Of the 7 closely associated cases 3 had squamous growths, 2 had undifferentiated growths, 1 had an adenocarcinoma and 1 a growth of unknown histology. In 4 other cases, a growth developed during the treatment of active pulmonary tuberculosis, in each case the tumour being closely associated with areas of active disease and this caused delay in diagnosis. All were squamous growths.

The association of these two conditions has been the subject of a number of studies. Statistics concerning the association are divided into those concerning the incidence of lung cancer in series of tuberculous patients and those

of the reverse pattern. Variability in published figures partly depends on the criteria used in the definition of tuberculous cases, particularly where necropsy reports are concerned. Muessle (1953), in a review of sixteen autopsy series from 1924-50, stated that active pulmonary tuberculosis occurred in 6.4% of lung cancer cases. Seyfarth (1952) found that in 1103 cases of lung cancer 11.42% had evidence of tuberculosis, the degree of activity not being stated. Sakula (1955), while reporting 6 cases of these combined conditions, quoted an incidence of 1.8 - 5.5% of pulmonary tuberculosis among lung cancer necropsies. Moll (1949) stated that "the association of the two conditions" might be as high as 8 - 10%.

The belief that the two conditions are mutually antagonistic, suggested by Rokitansky (1854) has no modern evidence to support it. The possibility that the two conditions coincide by chance is more likely but the proportion of 18 cases with evidence of tuberculosis among a series of 291 is, however, higher than would be expected by chance. A third possible explanation, that lung cancer predisposes to tuberculosis is unlikely as, apart from epidemiological reasons, most of the combined cases show the tuberculosis to have been present first and if a growth caused a local breakdown of host resistance one would expect the two conditions to be locally superimposed more frequently than they are. Although general host resistance to tuberculous infection might be reduced by the toxicity

caused by a growth, this would not be specific for lung cancer and might occur in any debilitating disease. The last possibility, that tuberculosis predisposes to the development of lung cancer has more evidence to support it and details of this have been given in the earlier section on aetiology.

Clinically and radiologically, the most important factor in determining the presence of a growth in a case of tuberculosis is the physician's awareness of the possibility of its occurrence. Clinical indications for suspicion quoted by Sakula are a worse general condition than would be expected from the degree of tuberculous infection, particularly in a male smoker over 40 years of age, unusual dyspnoea or persistent pain in the chest, failure to respond to specific therapy, excessive anaemia and sometimes a polymorph leucocytosis. Helm and Moon (1952) tabulated clearly and well the clinical and radiological differentiation, except that they described the wall of a neoplastic cavity to be thick with a ragged lining while quite a proportion of neoplastic cavities closely resemble the appearance of a tuberculous one. The commonest radiographic abnormalities which should cause suspicion are homogenous areas of atelectasis, an enlarged hilar shadow and an opacity, even when situated in the midst of others of characteristic tuberculous nature, which grows in spite of treatment or fails to respond in the expected manner. All those cases who, in this series, developed a growth while under treatment for tuberculosis had the radiographic picture of an opacity which grew in spite of

anti-tuberculous treatment. Two of these patients, while under treatment, developed a paralysed diaphragm (Plates 5 and 6) and this occurrence should give rise to suspicion of a co-existing tumour although in one case the tumour shadow did not enlarge until almost a year after the paralysis occurred.

TABLE 25

SYMPTOMS PRESENT AT FIRST HOSPITAL ATTENDANCE.

	Occurred in	% of total
Exertional dyspnoea	153	52.7
Productive cough	136	46.6
Increasing "	40	73.2
Dry "	37	
Haemoptysis	126	43.4
Loss of weight	113	38.8
Chest pain	86	29.6
Lassitude	69	23.8
Recent respiratory infection	21	7.2
Neurological (various)	12	4.1
Loss of appetite	12	"
Hoarseness	11	4.0
Malaise	9	3.0
Wheeze	9	"
Fever	5	1.9
Arthritis	5	"
Pain in back	5	"
Pain in epigastrium	5	1.9
Lump in neck	4	1.4
Swelling of face and neck.	4	"
Choking sensation	3	1.0
Vomiting	2	0.7
Pain in shoulder	2	"
Pain in arm	1	0.3
Pain in leg	1	"
Jaundice	1	"
Lump in axilla	1	"
Nocturnal dyspnoea	1	"
Palpitation	1	"
Dysphagia	1	"
Tightness in chest	1	"
Pallor	1	"
Diarrhoea	1	"

TABLE 26

FREQUENCY OF COMMON SYMPTOMS. PRESENT SERIES AND OTHERS.

Author	No. of cases in series	Exertional dyspnoea	Productive cough	All types of cough	Haemoptysis	Loss of weight	Chest pain	Lassitude	Respiratory infections
Present series	291	52.7	46.5	73.2	43.4	38.8	29.6	23.8	7.2
Brooks et al (1951)	502	10.3		41.9	8.7		16.5		
Ochsner et al (1952)	948	50		90	55	69	67	42	55
Gibbon et al (1953)	532	54	70	86	50	62	58	40	39
Victor (1955)	4117	40.1	54.4	73	45.1	48.5	53.8		
Rosenblatt and Lisa (1957)	210	47.6		75.2	33.8	59	43.3		

Figures are Percentages

TABLE 27

ANALYSIS OF PATIENTS WITH AND WITHOUT A HISTORY OF HAEMOPTYSIS.

	Haemoptysis present		Haemoptysis not present	
	No.	%	No.	%
Total number	126	43.3	165	56.7
Sex M/F	119/7		138/27	
No. under 60 years	50	40	93	56.4
Duration of symptoms				
Less than 1 month	16	12.7	16	9.7
1 - 3 "	50	39.6	55	33.3
4 - 6 "	25	19.8	47	28.5
6 - 12 "	23	18.2	33	20
over 12 "	12	9.7	14	8.5
Bronchoscopy	81	64.4	83	50.5
Proportion of those in whom positive evidence of growth obtained.	70	86.4	60	72.3
Histology of growth.				
Recorded	73	58	101	61.2
Squamous	49	67.1	42	41.6
Undiff.	16	22	39	38.7
Adenocarc.	5	6.8	17	16.8
Bronchiolar	3	4.1	1	1
Malig. adenoma	-		2	1.9
Site of growth.				
Recorded	122	95.2	154	93.3
R.M.B.	7	5.8	15	9.7
R.U.L.	26	21.3	41	26.6

CONTINUED

TABLE 27
(Continued)

ANALYSIS OF PATIENTS WITH AND WITHOUT A HISTORY OF HAEMOPTYSIS.

	Haemoptysis present		Haemoptysis not present	
	No.	%	No.	%
Site of growth				
R.M.L.	4	3.3	4	2.6
R.L.L.	23	18.8	27	17.5
L.M.B.	10	8.2	8	5.2
L.U.L.	32	26.2	36	23.5
L.L.L.	20	16.4	23	14.9
Peripheral growths	25	19.8	23	14
Resectable growths	19	15.1	33	20
Irradiated growths	36	28.6	13	7.9
radical	13	10.3	-	-
palliative	23		13	7.9

TABLE 28.

ANALYSIS OF PATIENTS PRESENTING WITH AND WITHOUT FINGER CLUBBING.

	Clubbing present		Clubbing not present	
	No.	%	No.	%
Total number	86	29.5	205	70.5
Sex M/F	83/3		174/31	
No. under 60 years.	30	34.8	109	53.1
Duration of Symptoms.				
less than 1 month	9	10.5	23	11.2
1 - 3 "	23	26.7	82	40.1
4 - 6 "	26	20.3	46	22.4
7 - 12 "	23	26.7	33	16.1
Over 12 "	5	5.8	21	10.2
Histology of growth.				
Recorded	50	58.2	124	60.5
Squamous	29	58	62	50
Undifferentiated	13	26	42	33.9
Adenocarcinoma	8	16	14	11.3
Bronchiolar	-		4	3.2
Malig. Adenoma	-		2	1.6
Site of growth				
Recorded	81	94.2	195	95.1
R.M.B.	6	7.4	16	8.2
R.U.L.	23	28.4	44	22.6
R.M.L.	1	1.2	7	3.6
R.L.L.	18	22.2	32	16.4
L.M.B.	5	6.2	13	6.7

CONTINUED

TABLE 28
(Continued)

ANALYSIS OF PATIENTS PRESENTING WITH AND WITHOUT FINGER CLUBBING.

	Clubbing present		Clubbing not present	
	No.	%	No.	%
Site of growth				
L.U.L.	20	24.8	48	24.6
L.L.L.	8	9.8	35	17.9
Peripheral growths	19	22	29	14.2
Resectable growths	13	15.1	39	19.0
Irradiated growths	14	16.3	35	17.0
radical	5	5.8	8	3.9
palliative	9	10.5	27	13.1

CHAPTER VI

RADIOLOGICAL FEATURES IN DIAGNOSIS.

Standard radiographic views; carcinoma of the middle lobe, bronchiolar carcinoma, pulmonary infarction. Fluoroscopy. Barium examination of the oesophagus. Tomography. Bronchography. Angiocardiography. Differential diagnosis.
Table 29.

References are made in this section to radiographic reproductions displayed in the APPENDIX. Plates 7 - 36.

Standard Radiographic Views.

The postero-anterior (P.A.) chest radiograph is undoubtedly the most useful single item in the diagnosis of bronchial carcinoma although the appearances of the growth can show wide variation. The initial radiological diagnosis, is moreover, not always

correct. In a survey of 501 cases of lung cancer in the Armed Forces, Lea (1952) found that 50.7% were correctly diagnosed at first radiograph; Bryson and Spencer (1951) stated that the initial X-ray diagnosis was correct in only 39.6% of their series of 804 cases.

The radiographic appearances of lung cancer can be divided into :-

(1) those due to the growth itself. In the early stages an isolated opacity, frequently round (one variety of "coin lesion") later a mass of increasing size which may undergo central degeneration, liquefaction and excavation, a central translucency then showing on the film. The growth may cast a very small shadow, the more obvious abnormality being infiltration which commences in the line of vascular or bronchial markings and indicating perivascular or peribronchial lymphatic spread.

(2) those due to secondary effects in the lung produced by partial or complete bronchial obstruction by a growth. If partial, emphysema is produced which may be localised to a subsegment or extend to a complete lung, if virtually complete there may be areas of atelectasis which vary from small linear shadows through collapse of pulmonary subsegments, complete segments and lobes up to a massive pulmonary collapse. With any degree of obstruction, retention of sputum occurs with the possibility of infection and resultant pneumonia showing as a dense opacity distal to the block.

(3) those due to secondary involvement of the regional lymph

glands. This causes enlargement of the hilar shadow, broadening of the carina due to the presence of glands below the bifurcation of the trachea and eventually, when mediastinal glands are involved, broadening of the mediastinum itself. McCort and Robbins (1951) reviewed the radiographs of 103 patients operated on for lung cancer and found to have regional lymph node metastases. They found enlarged nodes produced three radiological effects, (a) projection into the lung field of an enlarged glandular shadow, (b) alteration in contour of the mediastinum and (c) displacement of the mediastinum. The standard P.A. and Lateral film showed enlargement of lobar and interlobar glands but other techniques were required for paratracheal and bifurcation groups.

(4) those due to secondary deposits inside the thorax. It is comparatively uncommon for secondary neoplastic deposits to occur in the lung itself but when present they appear as opacities, usually circular, which rarely produce endobronchial obstruction. Pleural effusion due to involvement of the serous pleura by neoplastic infiltration either by direct extension of the growth or by lymphatic or vascular dissemination may arise, as may pneumothorax produced by perforation of the pleura by primary or secondary growth. Translucencies of varying size in the ribs or vertebral bodies, rarely the clavicles or sternum, and vertebral body collapse may occur.

It is generally agreed that radiological evidence of a growth is almost invariably present by the time that symptoms due to a bronchial carcinoma develop and that such evidence is usually present before there are any symptoms whatever.

This "preclinical phase" of lung cancer is a stage during which many authorities feel the growth is most amenable to surgical resection. Brocard, Choffel, Bouvier, Solignac and Ledu (1954) reviewing the subject stated that this phase may last up to two years.

The radiographic appearances during this early phase are important and have been described by several authors. Rigler, O'Loughlin and Tucker (1953) studied a series of 37 cases of lung cancer, all histologically proven, in each of whom a radiographic abnormality was present before the onset of symptoms. The earliest radiological changes in their series were :-

(1) a nodular density in the lung periphery.

(2) a solitary cavity or abscess in the lung periphery.

(3) an area of infiltration along the vascular trunks.

(4) unilateral enlargement of the hilar shadow.

(5) segmental, lobar or even unilateral whole lung emphysema.

(6) minimal areas of atelectasis, usually linear in type.

In a further review of films of cases eventually diagnosed as suffering from lung cancer in whom earlier films were available, Rigler (1952) found that the most common abnormalities missed on the earlier films were :-

(1) small peripheral nodules.

(2) unilateral hilar enlargement.

(3) localised emphysema.

In the present survey, there were twelve patients in whom a radiographic abnormality was present before the onset of

chest symptoms. Five were of the first type of Rigler et al with a nodular patch of increased density in the lung fields (Plate 7). In one of these cases secondary deposits of the same type were also visible in the film. Three patients were of the fourth type showing unilateral hilar enlargement (Plate 8). Two patients were of the sixth type showing areas of atelectasis. One other had consolidation in the right upper lobe and the last had a small peripheral shadow plus hilar enlargement. Thus, cysts and cavities were not noted in this presymptomatic group nor was localised emphysema but this is one of the more difficult abnormalities to spot and may pass unnoticed unless inspiration and expiration films are taken, or the patient screened.

Once symptoms have developed, a radiographic abnormality is almost always present. Zizmor (1955) while reporting two cases of lung cancer with apparently normal postero-anterior and lateral chest films, stated that a number of symptom-producing lung cancers with normal X-rays have been reported, quoting Rabin who found five such in a series of 200 cases of lung cancer. The fact that such cases are only occasionally reported in the literature shows that they are rare.

Table 29 sets out the radiographic appearances at the time of hospital consultation or admission in the present series.

The term "collapse consolidation" has been used in those cases where a shadow of varying size spreads out from the hilum, as these shadows contain elements of both processes. This was the commonest form of presentation (100 cases) and indicates that the main bronchi or the proximal portion of

the major bronchi are the commonest sites for the growth to develop (Plates 9 - 13). The isolated opacity of varying size with (Plate 7) or without (Plate 14) hilar enlargement was the next commonest appearance (67 cases) followed by more diffuse infiltrative shadows (37 cases) (Plate 15). Hilar enlargement was present in 98 cases altogether, in 31 of whom it was the only evident abnormality (Plates 16 and 17). Thirty two patients presented with the picture of a pleural effusion, in some cases the fluid obscuring completely the affected lung field. These patients did not necessarily have clear lung fields apart from the effusion but the effusion was the most striking abnormality in the radiograph (Plates 18 and 19). Definite abscess formation was seen in 11 cases the abscess cavity varying in site, size, contour, regularity and thickness of wall (Plate 20). Massive collapse (11 cases) indicated a complete collapse of one lung by obstruction of the main bronchus (Plate 21). A broadened mediastinum, due to involvement of mediastinal structures by secondary neoplastic growth was seen on 8 occasions, never as an isolated abnormality (Plate 22). Secondary deposits in the lungs were visible in 6 cases, an incidence of only 2.1% of the whole series (Plate 23). A pneumothorax was the presenting radiographic feature in one patient (Plate 24). Rib erosion by secondary growth was visible on the P.A. film in only 1 case, although other instances were uncovered by tomography. One case presented with widespread nodular shadowing.

Victor (1955) in a survey of 4,151 collected cases of lung cancer also found "atelectasis (massive or segmental)" the

commonest radiographic abnormality (62%) this being followed by "neoplastic infiltration (central or peripheral)" 38%, "hilar shadow" in 26% followed by less common abnormalities.

Carcinoma of the Middle Lobe.

Locke (1953) in his review of this subject found there were two common varieties. These were the peripheral type, a rather rounded tumour in a lobe of normal volume, and the central type, which caused segmental or lobar collapse. The second type was commoner and in his series bronchial occlusion was more frequently due to tumour than to pressure from glands. Of the 8 cases in the present series, 2 were of the peripheral, round shadow type, one of which was obscured by a pleural effusion and the other 6 were of the central type with resultant collapse-consolidation of the lobe. There were in addition several patients in whom a growth originating in other major bronchi had extended to block the middle lobe orifice.

Schwarcz (1955) reported the appearances of 14 cases of this condition seen between 1951 and 1954 in a Stockholm Hospital: 3 were of the massive infiltration type, 6 had massive infiltration and atelectasis of the lobe and 5 had small irregular infiltration and atelectasis. He found that the second group tended to be confused with encysted effusions and the third group with the middle lobe syndrome.

Bronchiolar Carcinoma.

The four patients with bronchiolar carcinoma presented

four different radiological appearances. The first (Plate 25) had heavy shadowing involving the middle and portions of the right upper and lower lobes which gradually increased in extent. The second (Plates 26 and 27) had a large pleural effusion with an underlying density occupying the middle lobe and portions of the right lower lobe. The third (Plate 28) had a hazy opacity in the right mid-zone involving all three lobes with a slightly raised right hemidiaphragm. The fourth (Plate 29) had a "snowstorm" lung with discrete opacities about 1 - 3 mm. in size covering both lung fields, coalescent in some areas.

Some authors state that the widespread nodular shadowing is the most common form of presentation (Shanks and Kerley, 1950; Decker, 1955). The latter found pleural effusion in 10% of his collected series of 155 cases. Storey et al (1953), in their comprehensive review of the subject, found widespread, bilateral, nodular shadows present in only 20% of cases when first seen, a figure similar to the present series. Over two thirds of the patients showed unilateral lesions on the first radiograph and 26% presented as a peripheral nodule, figures which again represent the findings in the present series.

Pulmonary Infarction.

Hanbury et al (1954) reported that in 10% of a pneumonectomy series radiographic shadows were seen in association with those caused directly by the bronchial carcinoma. On histological examination the cause was shown to be pulmonary infarction. These presented radiographically either as well defined peripheral shadows, as less well defined axillary

shadows or were completely obscured by the denser opacities of airless lung and other changes. These infarcts were not preceeded by venous thrombosis or embolism and appeared to be due directly to the presence of the growth although infiltration or compression of the main pulmonary arterial branches was found in only half the cases. If care is not exercised these shadows may be mistaken for secondary neoplastic deposits.

Fluroscopy.

The purpose of screening a patient with bronchial carcinoma is to determine the dynamic effect that the growth has on the normal appearance of the chest. The main points that can be ascertained are :-

(1) The size, position and movement, if any, of the tumour itself. Apart from movement, these are relatively unimportant as P.A., lateral and oblique radiographs will give the required information in a more permanent form.

(2) The presence of localised emphysema. This can often be seen better on screening than on inspiration and expiration films as can mediastinal movement on respiration.

(3) Movements of the diaphragm.

Apart from the tumour itself, paresis or paralysis of part of the whole of the hemidiaphragm is the commonest abnormality detected on screening. In this series, a record of screening was obtained in 120 cases. In 44 of these, abnormal diaphragmatic movement was noted varying from sluggish movement on respiration to gross displacement or complete paralysis with paradoxical movement on sniffing. Such diaphragmatic abnormalities result

from involvement of the phrenic nerve either directly by growth or more commonly by invasion of mediastinal lymph glands.

The causative growths were situated in these 44 cases as follows :- RMB 3, RUL 12, RML none, RLL 6, LMB 2, LUL 12, LLL 7 and site unknown 2. This shows the same relative distribution as the series as a whole, hence phrenic involvement was not related to growth in any particular lobe.

In those cases in whom histology was eventually obtained (19 out of 44 cases), the distribution was as follows :- squamous 9, undifferentiated 7 and adenocarcinoma 3. The numbers are too small to make valid deductions but the proportion of squamous growths is considerably lower than in the series as a whole.

Barium Examination of the Oesophagus.

The oesophagus can be displaced or deformed by secondarily invaded mediastinal lymph glands or even by direct extension of a bronchial carcinoma. It is not uncommon and in the present series records of a barium swallow examination were obtained in 78 cases of whom 28 (36%) showed an abnormality of the barium filled oesophagus. The commonest abnormality was a filling defect at the level of the lung hilum. Less common was displacement of the oesophagus to the contra-lateral side.

Middlemass (1953) in a series of 112 consecutive cases noted oesophageal distortion due to extrinsic pressure in 35 cases (31.2%). Most deformities, he found, were seen with the patients in the postero-anterior and left anterior oblique positions, and with the oesophagus both full and then barely

filled with barium. The most likely difficulty in interpretation was the alteration caused by an unfolded aorta.

The majority of the 28 patients with oesophageal abnormality in the present series had P.A. radiographs showing a hilar mass or the combination of a parenchymal mass and a broadened mediastinum. Four cases, however, had a normal hilar and mediastinal appearance on the P.A. film.

Although symptoms of dysphagia are usually due to massive infiltration of tracheobronchial and mediastinal lymph nodes causing compression, they can be due, according to Neuberger (1956) to passive hyperaemia of mucosa and even varicosities by compression of the oesophageal or portal veins. He stated that 10% of lung cancer cases showed post-mortem evidence of oesophageal involvement although only 3.8% complained of dysphagia.

In this series the incidence of symptoms in any way referable to oesophageal involvemant was 1.4%. The site of the causal tumour in the 28 cases was as follows :- RMB 2, RUL 8, RML none, RLL 7, LMB 4, LUL 6, LLL 1. Only 12 cases had the histological type of growth determined and they were as follows :- squamous 6, undifferentiated 3 and adenocarcinoma 3.

The numbers are too small to draw valid conclusions and the relative preponderance of adenocarcinomata and relative absence of left lower lobe growths could be due entirely to chance.

Tomography.

In this series tomography was performed in many cases and it contributed substantially to the diagnosis in 18 cases by the following methods :-

(1) Tomography of the primary shadow.

Determining the shape and extent of a lesion can usually be achieved on P.A., lateral and oblique radiographs, but the nature of the opacity may be more clearly seen on sectional films. Its peribronchial origin is often evident and additional nearby shadows or linear strands representing lymphatic spread stretching out from an opacity are sometimes seen. The demonstration of bronchial occlusion, partial or complete, is probably the most important single function of this examination. Four cases of this were seen in this series. A deformity of the vascular pattern may be well shown on tomograms.

The presence of central cavitation in a dense shadow is often unsuspected on a straight radiograph but tomography will reveal this (Plate 30). Even if it is obvious on a straight radiograph sectional films will reveal detail of the smooth or shaggy outline of the cavity, whether it is central or eccentric, the presence of any mass lying in the cavity itself, and the thickness of the cavity wall. Two cases in this series revealed unsuspected cavitation on tomography.

Calcification, its nature and extent, can be best seen on sectional films.

The detailed knowledge of the location and extent of a growth obtained by tomography is of value to the surgeon or the radiotherapist.

(2) Tomography of the mediastinum and hilar regions.

Greater detail of hilar enlargement can be obtained to help in differentiating between enlarged glands and vascular shadows. Four cases had doubtful hilar enlargement confirmed on tomography while in 2 others it showed involvement by growth of the lower end of the trachea. Tracheal displacement can also be well shown and help may be obtained in differentiating large mediastinal masses caused, for example, by Hodgkin's disease.

(3) Tomography of lungs apparently normal in standard views.

This can sometimes reveal the primary growth and this occurred in 1 case where lateral tomograms taken to confirm hilar gland enlargement revealed, in addition, the primary growth in the apex of the lower lobe.

It may also demonstrate the presence or absence of secondary deposits in the lungs. In 2 patients tomograms revealed, and in another patient confirmed, the presence of secondary deposits in the lungs (Plates 31, 32 and 33). Tomograms have in other cases confirmed that no abnormal shadows suspicious of secondary deposits were to be seen in the contralateral lung, a fact of vital importance when pneumonectomy was contemplated.

(4) Tomography of bones.

Bony erosion by direct involvement or by secondary neoplastic deposits may be visible on tomograms when

standard films have failed to reveal it (Plate 34). This is relatively uncommon in the spine but rib erosion can often be masked by a superimposed pulmonary opacity. All 3 cases of superior sulcus syndrome in this series had rib erosion and tomograms demonstrated this in 2 cases but failed to do so in the third in spite of the fact that at thoracotomy soon afterwards the ribs were in fact involved in the growth. Tomography is thus, not infallible.

Sectional films specifically taken to show bronchial obstruction are frequently taken with the patient lying at an angle which will bring the necessary bronchus into the plane of the X-ray table; Frain, Even, Roujeau, Marlois and Talamas (1955) recommended A.P. tomography of the trachea and main bronchi with the patient in a slight head-down tilted position and claimed this would show well any lateral displacement of the trachea, widening of the carina and presence of any glandular mass at the hilum. Locke (1953) advised a right posterior oblique position (40 ^{o} tilt) to demonstrate the length of the middle lobe bronchus and any associated glands.

In recent years, sectional films taken in a horizontal plane through the thorax, transverso-axial tomography, have been used. French authors have reported on this technique and Sichel, Forster, Roegel, Voegtlin and Lenz (1954) claimed some benefit from the technique in deciding whether a pulmonary mass had connection with the mediastinum and whether thoracotomy was likely to be of avail. Forster, Sichel and Roegel (1954) reported their studies on an unstated number of

cases and quoted three in more detail. They claimed that horizontal tomography gave considerable information which was reliable in tumours of the right hemithorax but not much help in tumours of the left hemithorax because the oblique position of the heart and aortic arch rendered interpretation difficult. It is unlikely that this method of examination will become popular for apart from the expense of new apparatus, the degree of accurate interpretation which can be achieved is unlikely to cause removal of the final decisions as to resectability of a tumour from the operating theatre to the darkroom.

Bronchography.

Filling the bronchial tree with radio-opaque oil is employed in the diagnosis of lung cancer primarily to demonstrate any bronchial occlusion. A series of lung cancer cases in which a bronchogram was carried out in every case in whom bronchoscopy had failed to demonstrate the growth was recently reported by Robinson and Pecker (1956) and, superior sulcus tumours and bronchiolar carcinomata excepted, they claimed the procedure was diagnostic in 90% of cases. The bronchographic abnormalities demanded for diagnosing a growth when bronchography was carried out to elucidate the nature of a peripheral shadow were :- (1) an abrupt arrest of the oil, transverse or oblique, smooth or irregular, concave or convex, or (2) a rat tail irregular defect or (3) a lateral irregular defect or (4) a missing branch. These findings were only significant if the other

segmental branches were well filled to the periphery and the affected branch was in the region of the abnormality seen in the plain film. False blocks by the presence of secretions in the bronchi occasionally cause difficulty in interpretation but preliminary postural drainage helps to prevent this. Robinson and Peckar stated that associated supperative pneumonitis of a lobe or a pulmonary abscess could usually be distinguished from a growth by the fact that they would show apparent blocks of several bronchi.

Bronchography was carried out in 13 cases in this series. In 9 cases a segmental shadow was seen on the straight films and a block of the appropriate bronchus was demonstrated in each case (Plate 35). In 4 cases a circumscribed peripheral shadow was seen on the straight films; complete bronchial occlusion was demonstrated in two cases (Plate 36), distortion of the segmental bronchus in one and poor filling of the segmental bronchus in another.

Demonstration of the nature of a bronchial occlusion in a peripheral lesion is valuable evidence but this does not apply to the same extent in segmental lesions where the source of obstruction is frequently within bronchoscopic range. Some authorities, however, prefer to have a bronchogram carried out before bronchoscopy, Kraus, Strnad and Ehbrecht (1954) claiming that more accurate localisation could thus be obtained and a more detailed bronchoscopic examination could be made of the affected area. This "directed bronchoscopy" was advocated by Huiginga (1952)

from Holland who stated that when bronchoscopy had failed to show a growth blind biopsy, preferably with a spoon curette, was more likely to contain neoplastic tissue in those cases in whom previous bronchography had demonstrated an abnormality.

The patient with unexplained haemoptyses who has apparently normal radiographs will sometimes be shown by bronchography to have a bronchial block caused by carcinoma. Zizmor (1955) has reported 2 such cases. MacHale (1953) reported an earlier series of 71 cases presenting with haemoptyses with no clinical or radiographic evidence of disease. Three of them (4.2%) were shown to have bronchial carcinomata by bronchoscopy and 1 who had a negative bronchoscopy was eventually shown to have a growth. The use of bronchography was not reported but it is probable that a combination of both procedures would reveal most abnormalities. Zheutlin, Lasser and Rigler (1954) described the bronchographic appearances in bronchiolar carcinoma and considered them almost diagnostic although their description would presumably not apply to the disseminated, nodular variety of the condition. As no bronchograms were carried out in the 4 cases in this series no criticism of their findings can be offered.

Angiocardiography.

The technique of angiocardiography in cases of primary and metastatic cancer of the lung was first discussed by Steinberg and Robb (1938). Opinions still vary as to the value of the procedure in this field. Novak (1956) described

the abnormal angiographic findings in 21 cases of bronchial carcinoma and stated that similar abnormalities were noted in cases of pulmonary sclerosis and fibrotic tuberculosis. Dotter and Steinberg (1951) published an excellent survey of its value with an account of the various abnormalities produced in the pulmonary and mediastinal vascular pattern by lung cancers and associated glandular secondaries. Both they and Slessor, Britt and Freer (1954) defined appearances which were considered as rendering the case inoperable.

No patient in the present series underwent this method of investigation.

With regard to the present position of this procedure, Dotter and Steinberg's final assessment will still serve six years later; "In the light of present knowledge, no patient should be denied exploratory surgery on the basis of angiocardiographic changes alone".

Differential diagnosis.

Reference has already been made in several Chapters to points in diagnosis. There is no doubt that the field covered in the differential diagnosis of lung cancer includes most diseases causing pulmonary abnormalities. The condition which caused greatest difficulty in the present series was pneumonia. It is a fairly generally accepted view that a pneumonia which remains unresolved after six weeks, in spite of treatment, particularly when occurring in a man over forty years of age, should be regarded with grave suspicion. Many cases in this

series were of this type. One drawback to the otherwise invaluable broad spectrum antibiotics lies in their ability to cause the resolution of pulmonary consolidation even when this is the result of partial endobronchial tumour obstruction. The persistence of a portion of the vanishing radiographic shadow in such a case was of serious import.

The difficulty of diagnosis in the presence of tuberculous infiltration has already been discussed. Another type of radiographic presentation which caused difficulty was the isolated round shadow, the "coin lesion". No estimation has been made of the number of such lesions due to all causes, seen during the period of the survey so no figure can be given of the proportion of "coin lesions" which were due to lung cancer. The figure has been quoted from 4.6% to 37% (Davis, 1956). The presence of a small amount of calcification in such a lesion does not exclude malignancy. These three types of radiographic abnormality, pneumonic consolidation, tuberculous infiltration and solitary "coin lesions" accounted for most of the problems in radiographic diagnosis but difficulty has been caused by many other conditions.

TABLE 29

RADIOLOGICAL APPEARANCE AT TIME OF FIRST HOSPITAL ATTENDANCE.

Appearance	Number of cases	
Collapse/consolidation	62	100
" " with hilar enlargement	38	
Isolated opacity	48	67
" " with hilar enlargement	19	
Diffuse infiltrative shadow	27	37
" " " with hilar enlargement	10	
Pleural effusion	32	
Hilar enlargement only	31	
Opacity with central abscess	11	
Massive collapse	11	
Broadened mediastinum	8	
Secondary deposits in addition to main shadow	6	
Pneumothorax	1	
Rib erosion in addition to main shadow	1	
Miliary mottling	1	

CHAPTER VII

A D D I T I O N A L D I A G N O S T I C P R O C E D U R E S.

Bronchoscopy. Exfoliative cytology. Pleural fluid examination. Pleural biopsy. Lung puncture. Biopsy of secondary deposit. Other miscellaneous investigations. Tables 30 - 39.

Bronchoscopy.

This is one of the most useful investigations as it can be carried out in the majority of patients with negligible mortality and with a good chance of providing definite evidence of the presence of a neoplasm. Table 30 compares the value of the method in the present series and those of Ochsner et al (1952) and Boyd et al (1954). It was carried out in only 56.4% of the present series, this low proportion being due to two factors. First, many patients with

advanced growths were seen and were too ill for the investigation to be carried out, whereas in any series reported from a surgical unit advanced cases are small in number, and second, in the early years of the survey facilities were such that bronchoscopy could be carried out only on those patients who were thought to be operable if a growth were thereby demonstrated. The type of patient rather than lack of facilities was the major of the two factors as is shown by the fact that among the 85 patients seen in 1955/56, only 49 were bronchoscoped, a rate that is still only 57.6%. The procedure gave evidence of growth in nearly 80% of the patients in whom it was carried out, rather higher than in series from surgical units. Aufses (1953) reported bronchoscopy to have a 65% success in a large series from a city community.

Barth and Kiessling (1956) reported a series of 480 proved cases seen from 1950 to 1955, and stated that positive bronchoscopy biopsy results in proximal tumours rose from 56% in 1950 to 96% in 1955 and from 14% to 40% in more peripheral tumours with an overall rate of positive diagnoses from biopsy alone of 80% in 1955. They attributed the improvement to the use of flexible biopsy forceps, modern anaesthesia and relaxant drugs. Robinson and Peckar (1956) in this country reported that positive evidence of growth was obtained in 50.8% of their series of 250 cases.

The reasons why bronchoscopy was not carried out in the present series are shown in Table 31. In the 164 patients who were bronchoscoped an abnormality considered malignant

was seen in 130 patients. In the remaining 34 patients, growths were subsequently found in the upper lobes in 24 cases (70%) and lower lobes in 10 cases (30%). This reflects the technical difficulty of viewing, and taking biopsies from, upper lobe growths.

The histological type of growth was identified by bronchoscopy in 102 cases as shown in Table 32. The comparatively small number of adenocarcinomata seen confirms the tendency of this type of growth to be sited distal to the main bronchi.

In the 43 cases subsequently undergoing resection procedures bronchoscopic evidence of growth was obtained in 83.7% (36 cases) compared with 25% in a surgical series reported from Philadelphia by Gibbon et al (1953), 63.7% in a similar series reported by Clerf and Herbut (1950) and 43.6% of the series of Robinson and Peckar (1956). In these 43 cases, regional glands were involved by growth in 20 (55.5%) of the 36 cases with bronchoscopic evidence of growth but in only 2 (28.5%) of the 7 cases where bronchoscopy was negative. The corresponding figures in Clerf and Herbut's series were 50% and 8%, thus indicating that although bronchoscopy is a very useful method of proving the diagnosis of lung cancer the absence of any positive finding should not necessarily lead to abandonment of the diagnosis for if a growth is present, it is less likely to have involved the regional glands.

Exfoliative Cytology.

The technique of examining specimens of fluid which have been in contact with neoplastic tissue or smears taken

direct from the neoplasm has been in use to an increasing degree in the last twenty years. There have been isolated reports of supposedly "neoplastic cells" being identified in sputum since Hampeln (1897) first reported their presence in the sputum of a case of bronchogenic carcinoma, but not until Dudgeon and Wrigley described their success in examining sputum for these cells (Dudgeon and Wrigley, 1935) was its value appreciated. A large amount of work has been done by Papanicolaou in establishing criteria for identification of exfoliated malignant cells. Four types of specimen are commonly used for this examination; sputum, pleural fluid, bronchial washings and smears taken direct from the growth usually by means of a polythene sponge. The second type requires a pleural aspiration and the third and fourth bronchoscopy but the first requires no more than the submission by a patient of a specimen of sputum. Hence, the popularity of this method.

The actual techniques used in fixing and staining specimens forthis examination are numerous. Dudgeon and Wrigley used Schaudinn-fixed wet film stained with Meyer's haemalum and counter-stained with eosin. Papanicolaou and Cromwell (1949) used ether-alcohol fixation followed by a complicated staining technique. A wet film methylene blue method was described by Jennings and Shaw (1953) and by Schuster (1955). The method used in Bedford is simple and less time consuming than most of those above, slides being Schaudinn-fixed and stained with haematoxylin and eosin. Examination for neoplastic cells has been carried out in

the latter years of the present survey in specimens of sputum, pleural fluid and bronchial washings. The pathologist has reported "Malignant cells present", "No malignant cells present", "? malignant cells present". In the latter case, cells have been seen which were suspected of being malignant, but if any doubt existed a "Malignant cells present" report was never given. Since 1950, specimens have been submitted from 126 patients and in 49 of these malignant cells were found. In a further 17 the presence of ? malignant cells was reported (Table 33).

Sputum. Malignant cells were identified in 40 of the 107 patients in whom sputum was examined (37.4%). The addition of 13 cases with suspicious cells brings the total success rate to 49.5%.

Pleural Fluid. The success rate based on 7 unequivocal findings among 16 patients was 43.7% and with 4 "probable" reports added, 68.7%.

Bronchial washings. This was carried out in only 3 cases and in 2 (66.6%) definite neoplastic cells were seen.

Thus neoplastic cells were positively identified in 49 of 126 patients in whom they were sought (39%). As no patient with a report of "? malignant cells present" was subsequently shown not to have a bronchial carcinoma it is reasonable to assess them in conjunction with the definite positives and this gives a total success rate of 52.5%.

Distribution (Table 34).

Of 58 cases in whose sputum or pleural fluid neoplastic

cells were identified and in whom the site of growth was localised it was found that practically all lobes were represented. The preponderance of positives from upper lobe growths is interesting and is in accord with the findings of Spjut, Fier and Ackerman (1955) in a series of 501 cases where the left upper lobe was, as in this series, the commonest source of "positive" sputum. In those patients with peripherally situated tumours in whom neoplastic cells were sought, 50% were positive. This is an important figure as bronchoscopy does not demonstrate these tumours. Bronchoscopy was positive in 68.9% of the malignant cell positive patients and in 72.7% of the negative patients, thus showing that the chances of obtaining a positive result to cytology is not affected by the site of the tumour. Jennings and Shaw (1953) found 64.3% positive cytology in 42 peripheral growths.

Type of Growth (Table 35)

This shows the types of growth from which the positive specimens were obtained. Identification of the histological type of the primary growth by examination of exfoliated cells has been achieved by many workers. Philps (1954) was correct in 10 confirmed cases and Umiker (1956) correctly typed 29 out of 31 cases. Spjut et al (1955) achieved an accuracy of 89.2% correct in epidermoid growths, 76.2% in undifferentiated growths and 39.3% in adenocarcinomata. Spriggs (1954) agreed with previously published figures and stated that squamous cells were most

commonly recognised and adenocarcinomata the least. He stated, however, that squamous cells are rarely seen in pleural effusions but they were present in 3 pleural effusions caused by squamous growths in this series.

Material for Examination.

Opinions vary as to the most reliable material to use, Herbut (1956) in a review of 1,000 cases stated that although sputum was the most easily obtained it was not as fruitful as bronchial secretions or washings obtained through a bronchoscope, owing to the presence of so many extraneous cells in sputum. Jackson, Bertoli and Ackerman (1951) claimed sputum to be better. Cahan and Farr (1950) reported the use of tracheal washings and aspiration, under local anaesthesia and nasal intubation, but the series was too small to give any conclusion as to the value of this method.

Reliability.

The reason why not all cases of bronchial carcinoma show malignant cells in the sputum is probably the simple one that there are so many sources of sputum other than the particular bronchus affected. The growth must communicate with a patent bronchus in order that exfoliated cells can be brought into the trachea. Buffmire and McDonald (1951) when studying the reasons for negative cytology in 51 cases of confirmed growths found that this was the cause in 67% of cases.

The reporting of "False Positives" should be nil if the investigation is to be considered absolutely reliable. Wandall (1944), McKay, Ware, Atwood and Harken (1948),

Liebow, Lindskog and Bloomer (1948), Woolner and McDonald (1949), Watson, Cromwell, Craver and Papanicolaou (1949), Jackson et al (1951), Jennings and Shaw (1953) and Zaman (1955) have all recorded the reporting of false positives in up to 12.5% of the number of true positive reports in their various series. In this series it is 3%. This consists of 2 cases, 1 of pneumonia and 1 a pleural effusion. Both reports were issued early in the series and on review, after greater experience had been gained, both were definitely considered not malignant.

The diseases with which the majority of false reports are concerned are bronchiectasis, chronic pneumonia, pulmonary tuberculosis, benign growths and pulmonary abscess. Bronchial metaplasia is the common feature. The presence in sputum of "Pap Cells" is now recognised. These are abnormal cells and are possibly exfoliated from metaplastic bronchial epethelium. They do not indicate malignancy. Papanicolaou (1956) reported the presence in some sputa of cells with certain degenerative changes referred to as "ciliocytophthoria" which might be related to bronchial carcinoma. "False positives" are likely to appear after the trauma of bronchoscopy and it has been suggested that no sputum should be submitted for 10 days after such event.

Number of specimens examined.

The number of specimens examined in each patient affects the degree of success in finding malignant cells.

Most writers agree that three specimens should be examined before a negative report can be given with reasonable accuracy. Jennings and Shaw claimed that six adequate specimens must be examined. They found malignant cells in 60.7% of their proven cancer cases but this represented 83.9% of those cases they considered adequately examined, i.e. with six specimens. The drawback to this is the very considerable time required for slide examination. Foot (1955) in his series of 1,000 cases, recommended that five positive reports should be obtained before thoracotomy was undertaken if there were no corroborative evidence on X-ray or bronchoscopy.

Table 36 shows the number of specimens examined from positive cases in this series. In sputum specimens reported positive, 66% were positive on one specimen examined, 84.9% on two specimens and 92.5% on three specimens. Thus examining three specimens produced over 90% of the positives reported. On the other hand the adequacy of examination of cancer patients in whom malignant cells were not found is shown in Table 37. This shows that 75.8% of the negative reports in sputum were based on less than three specimens per patient and were, therefore, by the better standards inadequately examined.

Value in relation to bronchoscopy.

Various authors have studied the finding of malignant cells in cases where bronchoscopy failed to show the growth. The proportion of bronchoscopically negative

patients who showed positive cytology has been given as 26% (McKay et al, 1948), 18% (Jackson et al, 1951), 28.8% (Clerf and Herbut, 1952) and 35% (Jennings and Shaw, 1953). In this series it was 30% if "definite positive" reports only are included and 53% if "probable positive" reports are added.

Summary.

There is no doubt that this examination, applied to sputum, is easy for the patient and physician, has a high degree of accuracy in capable hands, produces positive evidence of malignancy in about one half to two thirds of subsequently proven cases and can supply such evidence in over half the peripheral growths where bronchoscopy is least likely to help. Its main drawback is its time consuming character. In the hands of expert cytologists using only fresh specimens and using painstaking care in slide preparation and hours of microscopic study, accuracy to the order of 80% has been reported. As Papanicolaou and Liebow (1956) have pointed out, however, it is not how well it is done by cytological experts but how well it is done as generally practised.

It has been suggested that the most accurate results would be obtained by the appointment of a regional cytologist whose sole function would be to examine and report on specimens submitted from within his area. Such a system would have many advantages but it is doubtful if men prepared to accept such a limited field of work would be available.

A recent development was reported by Warfvinge (1956) who has published a preliminary report on over one hundred sputum specimens examined by paper electrophoresis. The patterns

obtained varied with different pulmonary diseases and it is possible that a pattern associated with carcinoma will emerge. A pattern associated with alveolar cell carcinoma was reported.

Pleural Fluid Examination.

Pleural effusion was present in 32 patients in this series when first seen at hospital but it developed in a further 34 patients during their illness, a total of 66 patients altogether, 22.8% of the series. In 20 cases no aspiration was carried out as the effusion was considered too small or was terminal. Of the other 46, 26 effusions were blood stained, 19 were opalescent and one was purulent. The cytology was not characteristic and eosinophilia was noted in only 1 case (vide infra, "Other Tests"). The examination of pleural fluid for malignant cells was the most important investigation when the diagnosis was in doubt and the findings have already been described. The site of the causative growth in the 62 cases where known is shown in Table 38. Apart from the fact that the proportion of growths in the main bronchi is higher than expected, the distribution is similar to that of the series as a whole. The histological type of growth of 39 cases where known is shown in Table 39.

This shows that the squamous growth is less likely than undifferentiated growths to produce an effusion probably because of its rather lower frequency of dissemination. As will be shown in Chapter VIII the prognosis of those patients presenting with a pleural effusion when first seen at hospital is poor.

Pleural Biopsy.

This has been advocated as a diagnostic measure and various methods have been employed. A thoracotomy can be performed in which case lung biopsy can also be carried out or a portion of pleura can be obtained by inducing an artificial pneumothorax and introducing a thoracoscope, though this is a procedure which can bear a considerable risk and has little justification nowadays unless a pneumothorax is already present. It was done in 1 case in this series. Obtaining a fragment of pleura by using an ordinary aspirating needle was first described by Craver and Binkley (1939) but the procedure was improved by Tripoli and Holland (1940) who used a Vim-Silverman biopsy needle for the purpose. Dutra and Geraci (1954) reported on its use and recommended that if there was any likelihood of a resection being possible, or even a thoracotomy to establish the diagnosis, the biopsy procedure was unwise owing to the risk of transplanting neoplastic cells along the needle track. Recently a report by Mestitz, Pollard and Purves (1957) gave further confirmation of the value of this measure, using a different type of needle. In over 60% of biopsies in a series of pleural effusions a firm histological diagnosis could be given.

The limitations of this biopsy procedure are that is is only safe when the lung is separated from the chest wall by fluid, thus preventing unintentional lung puncture, and that histological proof of malignancy can only be given if the needle strikes a portion of pleura which contains malignant tissue. In advanced cases this is quite likely but in an early

effusion a negative biopsy result in no way excludes the diagnosis of cancer. The procedure was carried out in only 1 patient in this series and malignancy was confirmed.

Lung Puncture.

This procedure is little used nowadays as the chances of obtaining a specimen of tissue satisfactory to the histologist is not high and the risks of a subsequent pneumothorax considerable.

Morrison and Deeley (1957) have reported the use of a hollow needle revolving at high speed for this purpose and by selection of cases to minimise the risks of pneumothorax were able to obtain a diagnostic report on the specimen obtained in 84% of a series of 36 cases. For technical reasons the needle can only be inserted a limited distance into the lung but within its limitations, if further experience fails to disclose any disadvantages such as secondary implantation, the procedure may well become more widespread.

Biopsy of Secondary Deposit.

This is a simple procedure when a palpably enlarged gland or a skin nodule is suspected of being involved in a malignant process. The diagnosis of cancer was confirmed histologically by this means in 12 cases in this series. The most commonly involved lymph glands are those in the supraclavicular fossa or the axilla. The frequency with which, during operations on the phrenic nerve, lymph glands were found in the pad of fat

which overlies the nerve at the root of the neck led to the use of gland biopsy from this area in the investigation of pulmonary disease. The use of scalene node biopsy, as it has come to be called, is increasing and diagnostic help can often be obtained. Daniels in 1949 reported the finding of malignant tissue in two out of five scalene node biopsies. Extrathoracic spread having been proved, thoracotomy could thus be avoided. By 1955, Skinner, Hall, Carr and Robbins could report on 100 cases of suspected lung cancer subjected to this procedure. Of 53 confirmed cases of lung cancer 24 showed histological proof in the gland. Positive results were obtained almost as often when no gland was palpable as when they were.

The value of the procedure lies in the fact that the operation carries virtually no mortality. If a negative report is obtained, no harm has been done and no subsequent procedure jeopardised; if a positive report is obtained then, as Daniels stated, an unnecessary thoracotomy has been avoided. It has even been suggested that in cases of bilateral pulmonary disease such as sarcoidosis, if a scalene node biopsy on one side of the neck fails then an attempt should be made on the other side. This would seldom be recommended in cases of bronchial carcinoma but in 1 case in this series, a bronchiolar carcinoma, a scalene biopsy on the right side was negative. At autopsy very soon afterwards a large scalene gland containing typical secondary bronchiolar carcinoma was present on the left side and though not palpable must have been present at the time of the right side attempt.

Other Miscellaneous Investigations.

There are a number of other minor procedures which are used to obtain more general information about the patient such as blood counts and erythrocyte sedimentation rate although these give no specific indication of a neoplasm.

Isaacson and Rapoport (1946) surveyed the occurrence of eosinophilia in patients with malignant disease. They stated that it occurred uncommonly but that when it did, and other causes for it could be excluded, it was indicative of metastatic dissemination and consequently indicated a poor prognosis. Over 90% of reported cases have shown the presence of metastases. Majumdar and Zahn (1957) reported such a case. The most likely of several aetiological theories is that it is an allergic response to the liberation of broken down protein from the primary growth.

Almost all lung cancer patients become anaemic during their illness this being attributed to infection, haemorrhage and malnutrition. Green et al (1957) claimed that this anaemia did not primarily result from the factors mentioned but was a true haemolytic anaemia. Liver function tests may assist in confirming the likelihood of tissue damage by secondary invasion but this may be gross before abnormal test results are obtained. Bone marrow studies may give a direct indication of neoplastic invasion of the marrow.

A study of the relationship between lung cancer and certain blood groups was reported by McConnell et al (1954). They confirmed the findings of Aird, Bentall, Mehigan and Roberts (1954) that the distribution of ABO blood groups was

the same as in control groups of other persons. They did find, however, a rather lower incidence of Rhesus negative individuals compared with the controls but the difference, though significant, was not great. Aird et al found no difference in Rhesus negative incidence between lung cancer cases and the general population. Blood grouping, therefore, has at present no useful value in the diagnosis of lung cancer although more detailed studies might yield some information on its aetiology.

No serological or excretion test has been discovered to give a firm indication of the presence of a pulmonary neoplasm, though Boyland, Gasson and Williams (1956) have studied the excretion of 5-hydroxytryptamine in the urine following administration of l-tryptophan. The resulting concentration was higher in patients with a cancer than in those without though lower than in patients with an argentaffinoma. As yet, the method is not helpful in the exact diagnosis of bronchial carcinomata. The most recent diagnostic test has been reported by Epstein and Sevag (1956) who studied the proportion of solid matter present in bronchial secretions. An arbitrary figure of 40% appeared to separate, with considerable accuracy, the cancer from non-cancer patients in the series. This test might come into use if further work supports the authors' findings.

In the present series, none of these mainly experimental methods of investigation have been used.

TABLE 30

RESULTS OF BRONCHOSCOPY. PRESENT SERIES AND OTHERS.

	Present series		Ochsner et al (1952)		Boyd et al (1954)	
	No.	%	No.	%	No.	%
No. of patients in series	291		320		403	
Bronchoscopy carried out	164	56.4	278	87	312	77.4
Positive findings	130	79.4	173	62	193	61.8
Biopsy taken	122	94	158	91	184	95.3
Positive biopsy	102	83.6	121	77	132	71.7
Proportion of positive biopsies in total no. bronchoscoped		62.3		43.5		42.3

TABLE 31

REASONS FOR NOT CARRYING OUT BRONCHOSCOPY.

Patient too ill or vena caval obstruction present.	53	Prevented by cervical arthritis.	1
Patient died too soon after admission.	12	Not proposed, diagnosis made only at autopsy.	2
Considered unnecessary as obvious secondaries present.	33	Peripheral pulmonary shadows considered out of range of bronchoscopic vision.	2
Patient refused.	12	Reason not known.	12

TABLE 32

HISTOLOGICAL TYPES OF GROWTHS IDENTIFIED ON BRONCHOSCOPY

Type	Number	%	% for series as a whole.
Squamous	65	64	52.3
Undifferentiated	28	27	31.6
Adenocarcinoma	8	8	12.7
Malignant adenoma	1	1	1.1
Total	102	100	100

TABLE 33

EXFOLIATIVE CYTOLOGY. FINDINGS ACCORDING TO ORIGIN OF SPECIMEN.

Origin of specimen		Definite Positive	Doubtful Positive	Negative	Total
Sputum	No.	40	13	54	107
	%	37.4	12.1	50.5	
Pleural fluid	No.	7	4	5	16
	%	43.7	25	31.3	
Bronchial washings	No.	2	-	1	3
	%	66.6	-	33.3	
Total	No.	49	17	60	126
	%	39	13.5	47.5	

TABLE 34

SITE OF GROWTH WHERE KNOWN IN POSITIVE CASES.

R.M.B.	R.U.L.	R.M.L.	R.L.L.	L.M.B.	L.U.L.	L.L.L.
5	11	-	9	3	19	11

TABLE 35

HISTOLOGICAL TYPE OF GROWTH WHERE KNOWN IN POSITIVE CASES.

Origin of specimen	Squamous	Undifferentiated	Adenocarcinoma	Bronchiolar carcinoma
Sputum	20	6	3	1
Pleural fluid	3	1	2	-
Bronchial washings	1	-	-	-

TABLE 36

POSITIVE CASES. PROPORTION OF POSITIVES OBTAINED BY SUCCESSIVE EXAMINATIONS.

Origin of specimen.		Number of examinations per patient						
		1st	2nd	3rd	4th	5th	6th	7th
Sputum	No.	35	10	4	3	-	-	1
	%	66	18.9	7.6	5.6			1.9
Pleural Fluid.	No.	9	2					
	%	81.8	18.2					
Bronchial Washings.	No.	2						
	%	100						

TABLE 37

NEGATIVE CASES. NUMBER OF SPECIMENS EXAMINED PER PATIENT.

Origin of specimen.		Number of specimens examined					
		1	2	3	4	5	6
Sputum	No.	20	21	7	2	3	1
	%	37	38.8	12.9	3.8	5.6	1.9
Pleural Fluid.	No.	5					
	%	100					
Bronchial Washings.	No.	1					
	%	100					

TABLE 38

PATIENTS WITH PLEURAL EFFUSION. SITE OF GROWTH WHERE KNOWN.

Site	R.M.B.	R.U.L.	R.M.L.	R.L.L.	L.M.B.	L.U.L.	L.L.L.
Number	8	14	1	9	6	10	14
%	12.8	22.6	1.6	14.5	9.7	16.2	22.6
% for series as a whole	7.9	24.3	2.9	18.6	6.4	24.6	15.3

TABLE 39

PATIENTS WITH PLEURAL EFFUSION. TYPE OF GROWTH WHERE KNOWN.

Type	Squamous	Undifferen-tiated.	Adeno-carcinoma.	Bronchiolar carcinoma.	Malignant Adenoma.
Number	12	17	6	2	2
%	30.8	43.6	15.4	5.1	5.1
% for series as a whole	52.3	31.6	12.7	2.3	1.1

CHAPTER VIII.

T R E A T M E N T A N D P R O G N O S I S.

Surgery; surgery in present series, operability, cases detected by M.M.R., survival of resection cases, inoperability, post-operative mortality, factors influencing survival after resection, lobectomy versus pneumonectomy, palliative resection, combined surgery and radiotherapy.

Radiotherapy. Palliative. Radical; factors influencing survival, supervoltage radiotherapy. Other therapeutic agents; radio-active isotopes.

Untreated patients; factors influencing survival.

Overall survey of treatment and prognosis.

Tables 40 - 52. Figures 2 - 10.

References are made in this section to radiographic reproductions displayed in the APPENDIX. Plates 37 and 38.

Surgery.

Until twenty five years ago, the treatment of bronchial carcinoma was confined to alleviating the patient's suffering largely with increasing doses of opiates. About this time Sauerbruch, Churchill, Tudor Edwards and Allen and Smith had each achieved a limited resection of lung tissue containing a malignant growth, with the limited success of extending their patients' lives by at least a year. In 1933 the first successful deliberate pneumonectomy for lung cancer was carried out by Evarts A.Graham, the patient having now survived over twenty years since the operation and in fact outliving his surgeon. Since then pulmonary resection has been carried out with increasing frequency and although the number of cures obtained has been relatively small, they greatly outnumber the patients with proven growths who have lived for more than a few years after diagnosis. It has thus become accepted that surgical resection of the tumour is the treatment of choice in a patient with lung cancer. Treatment by irradiation of the growth by X-rays has also been developed and accepted as being of some value though, as yet, not recognised as effective as resection.

The survey of the treatment used in this series of 291 patients has, therefore, been divided into sections dealing (1) with those who underwent pulmonary resection, (2) those who received radiotherapy and (3) with those patients receiving no treatment other than drugs for the palliation of

symptoms.

Surgery in Present Series.

Tables 40 and 41 show the number and type of operations carried out over the ten year period, in the treatment of this series of patients. There has been a fairly steady increase, the sudden jump in numbers in 1952 coinciding with the appointment of a regional thoracic surgeon. The majority of resections, 43 out of a total of 52, were pneumonectomies, 8 patients had lobectomies carried out and 1 patient a segmental (wedge) resection. The extent to which resection was possible in patients seen in different hospital departments can be seen by reference back to Table 19 (Page 83). The highest proportion of resections was among those patients picked up by M.M.R. (62.5% of such patients). Second highest (31.8%) was in those picked up by the practitioners' minifilm session. Next (25%) those under observation for other diseases though the number of cases is too small to be of value. Of the cases referred for consultation at the Chest Clinic 18.7% were resected while the worst rate (6.5%) was for those cases referred to other departments, the majority to general physicians. This poor figure is accounted for by the type of case which frequently presented with cerebral symptoms, obvious secondary deposits, jaundice, abdominal pain from liver enlargement, anaemia and other indications of advanced disease. The resectability rates followed closely the duration of symptoms which was lowest in the M.M.R. and 70 mm. film session cases.

Operability.

The proportion of patients suitable for exploratory thoracotomy depends upon the type of survey carried out. It is obviously high in material analysed from the records of a thoracic surgical department and lower in a general hospital where a considerable number of advanced and aged cases may be seen. Table 42 sets out the results of surgical series published in recent years. The majority of reports indicate that between one and two thirds of patients are suitable for exploratory thoracotomy. The figure for this area is lower, 25.1%, and this is probably a reasonable figure as the survey does not exclude any advanced cases as do some reports, and the majority of series quoted in Table 42 are based on cases referred to surgical departments. There has been some improvement over the years mainly due to the better surgical facilities after the first few years. The incidence of thoracotomies was 22% in the five years 1947/51 and 26.6% in the five years 1952/56.

The proportion of patients in whom a resection is carried out depends on the same factors as mentioned above. Table 42 shows figures of the proportion of resections carried out in patients subjected to thoracotomy, the percentage varying from 42 to 97.2 depending on the source of the material. Thus, about two-thirds of those explored have resection carried out. In this series the overall proportion was 71%, the lowest figure being 40% in 1949 and the highest 88% in 1955. Variation from year to year

is demonstrated in Figure 2.

The overall proportion of all lung cancer patients who undergo resection is about a quarter. Table 42 shows figures varying from 15% to 66%. Other figures are quoted by Smiley and Cheeseman (1956) 23%, and Mason (1949) 20.2%. This figure was usually about 15% before 1945 (Edwards, 1946) and had thus improved considerably over the past decade.

In the present series, the resectability rate was 13.5% for the period 1947/51 and 20.0% for the period 1952/56. The overall rate of 17.9% reflects the number of advanced cases included in the series.

Cases Detected by Mass Miniature Radiography.

The aim of this method of case finding is to detect the early asymptomatic patient. When such a patient can be diagnosed and referred for treatment quickly it is agreed by most authors that there is a very good chance of successful resection. The resectability rate in published series of M.M.R. detected cases varies from 22% (Denk, 1953) to 60% (Overholt, 1950; Bondi and Leites, 1952). It was 62.5% in such cases in the present series. The average is thus higher than in the usual series of cases derived from different sources.

There is often, however, a considerable delay in getting these patients to surgery. Overholt, Bougas and Woods (1955) reported 46 "silent lung cancers" picked up by M.M.R. with an average delay from radiograph to therapy of six months,

by which time 39% had developed symptoms. In this series just over one third of the M.M.R. cases did, in fact, have symptoms when seen at hospital. One reason for the failure of this method of detection to give consistently better surgical results is that growths which are big enough to show on radiographs but are not producing symptoms are usually peripheral and such growths may metastasise before treatment can be instituted.

Survival of Resection Cases.

In the period under survey, 52 patients underwent pulmonary resection. Survival times have been calculated from the date of operation. The follow-up extended to November 1957. Of the 38 patients with a complete follow up of five years 7 died within 1 month of operation, 10 between 1 and 6 months, 9 between 6 and 12 months, 8 between 1 and 2 years, 2 between 2 and 3 years, none between 3 and 4 years and 1 between 4 and 5 years. One patient survived over 5 years. Of those 14 patients still living but who have been operated on too recently for a full five year follow-up to be completed, 2 are living between 1 and 6 months after operation, 2 between 6 and 12 months, 3 between 1 and 2 years, 1 between 2 and 3 years, 1 between 3 and 4 years and 5 between 4 and 5 years. As the numbers concerned are small and nearly a quarter of the total have an uncompleted five year follow-up, the survival rates have been calculated by the Life Table Method (Figure 3). This method applies to the patients still alive the monthly or annual mortality rates derived from analysis of those

patients who have died. As those patients with incomplete follow-up have all had their operations in the last few years when improvements in technique are known to have occurred, the calculated survival rates probably give too pessimistic a picture. Thus, although only one patient has lived 5 years after operation there are five others who are all within a few months of reaching their fifth post-operative anniversary and each is well and might justifiably be expected to reach it. This would change the 5 year survival rate in the Life Table analysis from 11% to 19%. During the first post-operative year 53% of the patients died, during the second year 20%, in the third year 5%, in the fourth year 0%, and in the fifth year 11% or if the assumption mentioned above were accepted, 3%. Thus, the majority of deaths after operation occur in the first year, an appreciable number in the second year, less in the third year and few thereafter. As no allowance has been made for deaths from other causes, it would appear that few deaths from carcinoma recurrence or secondary deposits occur after the third anniversary. Three year survival rates would give, therefore, almost as accurate a picture of the results achieved by surgery as five year figures. There were 8 three year survivors out of 35 patients operated on before November 1954, an actual rate of 22.8%. This coincides closely with the Life-Table estimated rate of 22% at three years. Table 42 includes a number of recent three and five year survival rates. Three year rates vary from 22.4% to 33.3% with an average of 28%. Five year rates vary from 13.7% to 33% with

an average of 23%. The Life Table figure for the present series is 22% for three years and 11% for five years but as mentioned earlier, this might well be 19% after a few more months. The local overall figures are slightly lower than the general results and reflect the fact that surgery has been attempted on all patients with the slightest chance of a successful operation.

Inoperability.

If it is believed that surgery offers the best hope of cure, it should be advised in all cases where hope of successful resection can be entertained. The presence of certain clinical features are now considered to reduce this chance of success. Reasons why certain patients in this series were considered inoperable are given in Table 43.

(1) Detectable extrathoracic metastases. With the exception of a single resectable secondary deposit, the presence of these renders the vast majority of such cases inoperable. Possible exceptions are those patients with gross pulmonary sepsis best treated by resection and occasionally a patient with severe pain from pulmonary osteoarthropathy. Only one patient in this series had a resection in the presence of a known extrathoracic metastasis, a deposit in the cerebrum. The result was a failure as the cerebral deposit became inoperable before its removal could be attempted.

(2) Poor general condition and poor pulmonary function.

These are factors which in borderline cases are largely indefinable except in the individual surgeon's personal judgement.

(3) Malignant pleural effusion. This is usually accepted as a contra-indication to operation (Boyd, 1954). Four patients were operated on in this series in the presence of a pleural effusion. Two died within 3 months, one is living 9 months and the other 2 years after operation. In neither of the latter two cases had neoplastic cells been detected in the effusion.

(4) Laryngeal nerve paralysis. This indicates extra-pulmonary spread of the growth and therefore almost certainly eliminates the possibility of complete removal of malignant tissue at operation. Opinions vary, however, as to the advisability of surgery in its presence. Gibbon et al (1953) stated that such cases have a very bad prognosis and are inoperable while Ochsner et al (1952) claimed that it did not necessarily preclude resection. No such cases were operated on in this series.

(5) Phrenic nerve paralysis. This has a similar implication, but is not considered to be such a definite contra-indication as laryngeal nerve paralysis. Three patiants with proven phrenic nerve involvement in this series had resections. Two died within 6 and one within 12 months of operation. In each case the hilar and mediastinal glands were involved.

(6) Chest wall involvement. This does not preclude

operation but considerably reduces the patient's chance of worthwhile survival.

(7) Growth near the carina. Not uncommonly the growth is seen bronchoscopically to invade the carina and this renders the tumour quite inoperable. Visible growth in the proximal portion of the stem bronchus or in the opposite lung have a similar import.

(8) Superior vena caval obstruction. This is evidence of considerable mediastinal involvement and is a definite contraindication.

(9) Abnormality of the oesophagus as shown by barium swallow is sometimes taken as an indication of inoperability. In the opinion of Middlemass (1953) if the growth were visible on bronchoscopy, oesophageal change, even if minor, probably indicated inoperability whereas if the growth were not visible, the significance of oesophageal change was more doubtful. Others have stated that a barium swallow is of little help in assessing operability (Slessor et al, 1954). In this series resection was carried out in 5 such cases. All had enlarged hilar glands, some had enlarged mediastinal glands as well and all but 1 died within one year, the remaining 1 being still alive eighteen months after operation. Thoracotomy carried out on 3 other patients revealed mediastinal involvement too extensive to permit resection.

Taylor and Waterhouse (1950) found that over 10% of patients had evidence of extrapulmonary spread from the onset of their presenting symptoms and Oswald (1956) found that, at

the time of diagnosis, the growth was apparently limited to the lung in 51%, had spread to the mediastinum in 23% and spread beyond the thorax in 26%. In this series, of the 239 non-resectable patients (Table 43), 31.5% had no resection because quite irrespective of the extent of the growth the patient's general condition and/or poor pulmonary reserve precluded it, 32.9% had considerable extra-pulmonary, though intra-thoracic, spread of growth and 23.9% had extra-thoracic spread. The remaining 11.7% consisted of those patients who refused operation or were not diagnosed until after death.

Age, per se, is not strictly a contra-indication but the factors which are included under the broad heading of "Poor general condition and/or pulmonary reserve" occur with increasing frequency as age advances with the result that few patients over the age of seventy years and very few over eighty are accepted as reasonable surgical risks. These factors include toxicity, poor myocardial reserve even in the absence of overt cardiac failure, hypertension, evidence of cerebro-vascular damage, poor renal reserve and, very commonly, poor respiratory function resulting from chronic bronchitis and emphysema.

Post-Operative Mortality.

There is no set period of time which is accepted as the post-operative phase and deaths within periods varying from seventy two hours to three months after operation have been classified as post-operative deaths by different authors.

The exclusion of post-operative deaths when estimating survival rates is a feature of some published series and this certainly flatters the success of the surgeon, but such deaths must be accepted as part of the risk of operation and should be included in analysis. Published rates have one great value in that they demonstrate clearly how post-operative mortality has dropped since pulmonary resection was first undertaken. This is shown in Table 44 and it is obvious that since 1946 the operative mortality in the U.S.A. and Britain is almost half what it was prior to that date. The improvement can be attributed largely to the fact that more early cases are coming under the surgeons' care and to the great advances in surgical and, particularly, anaesthetic techniques. The overall mortality within one month of operation in this series was 13.4%.

Comparative figures for pneumonectomy and lobectomy in addition to those of Churchill, Sweet, Soutter and Scannell (1950) quoted in Table 44 have been given by Gifford and Waddington (1957) as 25.9% and 14.7% respectively. In a collected series of lobectomies (Belcher, 1956) the figure was 10%. In the present series, only 8 lobectomies were carried out and none died within three months of operation. The mortality rate among resections where no spread outside the lung has been demonstrated is lower than among those where more tissue than the lung itself has to be removed. Frkovich, Robertson and Gourlay (1956) quoted an overall surgical mortality of 13% (within 72 hours of operation); the rate for "curative

resections" was 8.5% and for "palliative resections" was 17%. In this series the mortality rates one month after operation for equivalent cases were 17% and 12%, the reverse of what was to be expected. The deaths among palliative resections increased, however, and six months after operation more of these cases had died than those with curative resections, thus confirming the expected results as quoted by Frkovich et al.

Factors Influencing Survival after Resection.

(1) Duration of Symptoms. It was pointed out by Bignall and Moon (1955) in their analysis of 531 cases that the 2-year survival rate following surgery was highest in those patients who had symptoms for over a year before operation. The next highest rate was in those patients with symptoms for less than three months and worst in those with symptoms lasting from six to eight months before operation. This paralleled the findings of Bignall (1955) in untreated lung cancers. The findings in operation cases were not due to a preponderance of squamous cell growths in the longer living groups and it would seem that the risk of dissemination of the growth is greatest in patients with a six to nine months history. These findings were confirmed by Gifford and Waddington (1957) in a study of 2,156 cases admitted to the Liverpool thoracic surgery departments. Patients with histories of over nine months had the best survival rate, next best were those with histories of under six months and the worst rate in six to nine months histories. This applied to both 3 and 5 year

survival rates. Unlike Bignall and Moon's findings there was a higher proportion of squamous growths among the groups with better survival rates. Nicholson et al (1957) in a study of 910 cases seen in Manchester found no relationship between length of history and survival. In those patients in the present series with a 2-year follow-up the findings are shown in Table 45. The 2-year survival rates follow the pattern of the first two series quoted above. Like Bignall and Moon, the proportion of squamous growths did not follow the trend of survival rates.

(2) Site of Growth. There is little evidence to indicate a marked prognostic difference in patients with growths in the right or left lungs or in the upper or lower lobes. Bignall and Moon found the prognosis better in upper lobe growths but Nicholson et al found the reverse while Gifford and Waddington found the right lower lobe to be the site with the best 5-year survival rate. Belcher, in his survey of lobectomies stated that prognosis is unrelated to the tumour site. Again, Holmes Sellors considered that patients with centrally placed growths had the best survival while Ochsner in earlier years had found the opposite. The number of patients required to make any accurate assessment of the prognosis of growths in different sites is very large as many other more important factors must be taken into account. The number of patients in this series is too small for such an analysis.

(3) Involvement of the chest wall. This obviously reduces the chances of complete clearance of the growth.

Gibbon et al (1953) found that no resection patient lived longer than eighteen months after operation if the chest wall had been involved. Gronquist et al (1957) followed 16 such cases at the Mayo clinic. Ten died within fourteen months of operation and of those still living, 2 survived two post-operative years but only the parietal pleura had been involved. In this series 5 patients had resections in the presence of chest wall invasion. They died 3, 5, 5, 9 and 20 months after operation.

(4) Involvement by growth of the regional lymph glands. This definitely reduces the length of survival. Table 46 sets out a number of published figures and these all show the difference, very marked in some series, between the survival rates for patients undergoing "curative" resections in whom the growth is apparently confined to the lung at operation and those undergoing "palliative" resections where local extrapulmonary spread has occurred before operation. Figure 4 shows the Life Table survival curve for the patients in this series, 18 of whom underwent "curative" resections and 34 "palliative" resections. The former group contains 5 patients only a few months short of their fifth post-operative anniversary and if they reach it, and all are at present well, the five-year survival figure would be raised from 26% to 45% a figure which compares favourably with the published results in Table 46. No patient in the "palliative" resection group has lived more than four years after operation although 6 still survive from six months to three years after operation but some of these already

show evidence of recurrence.

(5) The histological type of growth. It has been noted in many surveys of resection cases in the last decade that the prognosis in squamous cell growths is better than in other histological varieties. This, however, has not been a universal finding, several authors stating that adenocarcinoma cases had the best prognosis. Bignall and Moon (1955) found this as did Belcher (1956) in his collected lobectomy series. Aufses (1953) gave a "cure rate" of 31% in adenocarcinomata, 20% in squamous growths and 9% in anaplastic growths. Gifford and Waddington (1957) found adenocarcinomata had the worst prognosis in their series. This discrepancy is probably due to the fact that the most important single factor in prognosis is whether or not the regional glands have been invaded by tumour at the time of operation and not on the type of tumour itself. Aufses explained his findings by the fact that the majority of the adenocarcinomata were circumscribed growths and tended to be peripherally situated and this circumscribed type of tumour had twice the cure rate of main bronchi or peripheral invasive tumours. It is much more certain that undifferentiated growths have the worst prognosis, Toft (1955) even stating that operation on anaplastic tumours was of doubtful value. Overholt and Bougas (1956a), however, had 7 oat cell growths among 46 five-year survivors so the outlook, if no obvious dissemination has occurred by the time of operation, is by no means hopeless. Such dissemination is early in undifferentiated growths and therefore excludes many

afflicted patients from resection, so the overall outlook for such patients is poor. In the present series the number of patients is too small to make an accurate analysis as the factor of extrapulmonary spread cannot be eliminated. Of 44 patients with well defined histology there were 30 squamous growths, 10 undifferentiated and 4 adenocarcinomata. With 4, 2 and 1 three-year survivors, the respective survival rates are 13.3%, 20% and 25% which places squamous growths with the worst outlook contrary to the findings in larger series.

Storey et al (1953) in their survey of 153 cases of bronchiolar carcinoma found the surgery rate very low on the whole but when resection was performed and the patient lived 2 years the outlook for further survival was good. The prognosis in this type of growth is, therefore, poor as its distribution makes surgical treatment very infrequent but when possible the results are comparable with those in other lung cancer types. No such patient was operated on in this series.

(6) Sex. The number of women in resection series is usually small and often no comment is made on the influence of this factor. Bignall and Moon (1955) in their resection survey found the prognosis better in women, with 2-year survival rates of 65% and 46% for women and men respectively and 5-year rates of 57% and 31% but as the number of women was small, no firm conclusions could be drawn. In the present series only two women underwent resection, one dying 5 months later and the other is still alive 2 years later. The operability of women in the series was low, 6% of all women seen in ten years compared with 19.5% of men.

(7) Age. Apart from the fact that old age brings with it medical conditions which render operative procedures more risky than those undertaken in younger patients, the factor of age is not important. Gifford and Waddington found the age group 55 - 59 years had the lowest pneumonectomy mortality and best survival record while Jones et al (1955) found the highest resectability rate in the 60 - 64 years group. The present series of 52 is too small for accurate analysis. Holmes Sellors in his analysis found that the respiratory reserve of the patient was of cardinal importance in estimating resectability, a finding in common with other surgeons. It certainly has an effect on the quality of life after resection if not on its actual duration. He attached little importance to the size of the tumour and this is also the experience of others, the site and invasive nature being much more important than mere size.

(8) Extent of Operation. Lobectomy has come increasingly into use in the surgical treatment of lung cancer, the results in selected cases being good, some of these being described below. Brock and Whytehead (1955) have described their results in a series of radical pneumonectomies. This is an extensive operation with clearing of regional glands and intrapericardial ligation of vessels. They claimed that the mortality was no worse than in simple pneumonectomy and it gave better survival results. Thus, operations varying in extent from simple lobectomy to radical pneumonectomy are employed and it will probably never be possible to describe any one type of operation as that yielding the best prognosis, the factors

involved being so numerous.

Lobectomy versus Pneumonectomy.

It is axiomatic that in any operation involving pulmonary resection the smallest amount of healthy lung tissues should be removed compatible with achieving the desired result. When dealing with lung cancer it was often impossible to define at operation the limits of the growth and it became necessary for surgeons to remove the entire lung in order to ensure as near complete excision of the growth as possible. Thus, pneumonectomy became the standard operation. Some authors, such as Brock and Whytehead, advocated extensive excision in all cases. Ochsner and his colleagues in 1952 advised pneumonectomy or nothing. Other surgeons have, however, found that more limited resections could produce good results. Overholt and Bougas (1956b) found that pneumonectomy gave no better survival than deliberately chosen lobectomy. Aufses (1954) found a five-year survival rate of 26% among 53 lobectomies compared with 17% in 112 pneumonectomies. Boyd et al (1954) quoted their "average survival" after resection as 27.9 months; after pneumonectomy it was 23.3 months and after lobectomy 32.5 months. The crucial point in the controversy was outlined in the survey of Bignall and Moon (1955) whose findings were that the survival rate was better after lobectomy than pneumonectomy but that the lobectomy series included fewer cases with hilar gland involvement. When all the cases with no hilar gland involvement were analysed the survival rate was equal in the two operation groups. Belcher (1956) surveying

a series of 264 lobectomies performed by a number of surgeons, found survival rates above average for general resection series. The percentage of cases with regional gland involvement was low, only 27%, and this might account for the good figures.

Thus, opinions still vary as to the advisability of performing lobectomy as a deliberate policy in cases of lung cancer. Where the growth is localised, such as a small peripheral growth, and where the regional glands are not involved the results appear to be good and there is certainly a smaller loss of functioning lung tissue which might make a considerable difference to the patient's comfort. It is possible that as the lymph drainage from each pulmonary lobe becomes known in greater detail (q.v. the work of Nohl, 1956) the operation of radical lobectomy may be practised with increasing confidence.

Palliative Resection.

As stated earlier, 34 patients underwent resection which could be described as "palliative" in that the growth had extended beyond the lung. This is justifiable when there is a reasonable chance of excising the involved mediastinal structures. When this is considered to be impossible resection is still justified in a few cases. It is worth while when there is considerable septic absorption from the involved lung from, for example, a large neoplastic abscess. It is often successful in the patient suffering acutely from the pain of hypertrophic osteoarthropathy which is usually relieved

within hours of resection. Vagotomy or hilar denervation are lesser procedures which may be successful for this particular purpose if resection cannot be attempted. Two such patients in the present series underwent pneumonectomy, one dying on the third post-operative day while the other lived for seven months with very considerable remission of joint symptoms. Very occasionally, resection may be justified in the presence of extensive intrathoracic secondary deposits for psychological reasons but no such case occurred in this series.

Combined Surgery and Radiotherapy.

Reported series have given little encouragement to the policy of combining both resection and radiotherapy in the treatment of bronchial carcinoma. The survival of patients treated with resection first and irradiation second was not significantly different from those of surgery alone. The reversal of the order of the two treatments held out more promise of improved results. When operation was performed after the growth had been irradiated it was often found that the growth had diminished in size and was in some cases reduced almost to an area of fibrosis. Bromley and Szur (1955) reported a series of 66 patients treated by this combined method. Immediate results of surgery were good inasmuch as the tumour was irradicated from the chest in nearly half the cases. There was a disturbingly high incidence of bronchopleural fistulae and empyemata, however, which the authors considered were due directly to the pre-operative irradiation causing

changes in the bronchial wall. The technique was considered inadvisable on these grounds.

In the present series radiotherapy was used after resection in 6 cases; in 3 because at operation mediastinal glands were seen to be involved and could not be entirely excised, in 1 because at operation the chest wall was found to be invaded and in 1 apparently as part of a policy in force at that time in the surgical unit concerned. In 1 case where a secondary deposit was noticed in the left lower lobe it was irradiated after the right lower lobe containing the primary growth had been excised. In 1 patient in this series pneumonectomy was carried out after a course of radical radiotherapy. No bronchopleural fistula developed but the patient died of metastases four months later. Survival periods ranged from 2½ months to 4 years 7 months in the patients with combined therapy. The numbers are too small for accurate analysis.

Radiotherapy.

The destructive effect of X-radiation on the human cell has been employed since the beginning of this century in attempts to destroy the cancer cell. This can be achieved by a sufficient concentration and duration of rays but the difficulty has always been to spare the normal tissue surrounding the growth and to minimise the resultant effects on the patient as a whole. Irradiation of lung tumours can produce effects such as oesophagitis, bone-marrow depression and skin burning. Modern methods have minimised these effects by better selection of patients, the use of multifield and grid techniques and the concomitant employment of drugs found to alleviate the more distressing symptoms of nausea, vomiting and depression. The development of more powerful radiotherapy machines has probably been the greatest single factor and this has been brought almost to the possible limit in the Linear Accelerator and Cobalt Bomb producing a power of up to eight million volts compared with a quarter of a million of the conventional machine.

The actual method by which irradiation kills a tumour is not precisely known. It may be by direct action on the mitoses which are a cardinal feature of a malignant process. Pannett (1957) suggested that the effect was on the healthy tissue surrounding the tumour, thereby producing or altering some substance which passed into the tumour by the lymph channels and he cited some evidence to support the theory. Whatever the method, there is no doubt that irradiation can

result in the partial, if not complete, destruction of a malignant growth and some of its secondary spread. The greater the amount of irradiation given to any patient the greater is the destruction of the growth but so is the deleterious effect on the patient as a whole. It has come to be recognised, therefore, that radiotherapy can be used in two broad groups of persons; firstly in those with moderate or advanced disease in whom it has been found by experience that only temporary relief of symptoms can be achieved (Palliative Radiotherapy), and secondly in those with less advanced disease who are fit enough to stand the rigours imposed by a considerable amount of irradiation and in whom complete destruction of the malignant process is the aim (Radical Radiotherapy). No comparison can, therefore, be made between the results of treatment in these two groups.

In all, 59 patients in this series received radiotherapy, 42 a palliative course (14.1% of the total series) and 17 a radical course (5.8% of the total series). They included 8 women and 51 men. Forty four of them had the growth confirmed histologically. Table 47 and Figure 5 show the histological types of growth involved and the survival rate. It can be seen that the majority of patients living longer than 1 year after treatment and all those living longer than 2 years had squamous growths. The average survival time of the dead patients was 6.5 months; six patients are still living, 12, 14, 16, 16, 20, and 34 months after treatment. The median survival time (the time taken for half the

patients to die) was 4.8 months.

The aim of treatment in the Palliative and Radical groups was so different that the figures for each will be discussed separately.

Palliative Radiotherapy.

The aim of this form of treatment was not primarily to prolong life but to improve the quality of the patient's remaining life. The total dosage of irradiation used was between 2,000 and 4,000 r and the duration varied from a few days to a month. As the patients usually had advanced growths and their general condition was poor and as even a palliative course could produce unpleasant side effects, the use of palliative radiation was usually restricted to those patients with particular symptoms from which relief could be expected. These particular conditions are fairly generally accepted as follows :-

(1) Superior vena caval obstruction. Ten patients were treated for this condition. All patients were benefited. In four the condition recurred before death, in the others it did not. This complication of bronchial carcinoma above all others is the one most likely to be benefited by radiotherapy. Its presence renders the patient inoperable and unsuitable for radical treatment but it is considered nowadays as a radiotherapeutic emergency requiring immediate admission to a suitable hospital. Szur and Bromley (1956) obtained relief in 69% of such patients, 80% of them dying

before evidence of further obstruction had appeared. In the present series, of 15 patients with this condition who received no radiotherapy 4 died within one month of its onset and all were dead within six months. Of 10 similar patients who were treated 7 died within six months, 2 died within the next six months and one lived over a year. It can be seen that life is prolonged slightly with treatment but treated or not, the majority of patients with this syndrome die within six months. The value of treatment lies in the relief of discomfort and not in extending life.

(2) Haemoptysis. This syndrome is relieved in the majority of cases. In a series reported by Blanshard (1955) it was improved in 64%. Ten patients with haemoptysis in the present series were treated, with relief in a few cases. Follow-up details of the patients are insufficient to give accurate figures of those obtaining relief of this symptom and of others mentioned below.

(3) Pain. The effect of radiotherapy on pain depends upon the cause of the pain. When it results from secondary deposits in bone it usually responds well. When due to local invasion by the tumour the results are usually very poor indeed. Blanshard found that a midline pain radiating through the middle of the chest which he described as "Mediastinal Pain" was relieved in every case.

(4) Cough. This is diminished in 50 to 75% of patients when the cough is caused by the presence of the tumour. Dyspnoea and dysphagia are alleviated in a similar percentage

of patients where the major cause is the presence of a growth. In this series no patients were treated primarily for dysphagia but in three patients in whom it occurred in association with superior vena caval obstruction it was relieved.

With proper selection of cases over half the patients treated with palliative radiotherapy can be expected to be benefited, although Brown (1952) reported the effect lasted less than three months in half his cases.

In this series the histological type of growth and survival is shown in Table 48 and the Life Table survival in Figure 6. The average time of survival after treatment in the dead patients was 5.4 months. Three patients are still alive, 11, 14 and 20 months after treatment. The Median Survival Time was 4 months. To show that the survival pattern in this series is similar to the more comprehensive surveys carried out by radiotherapy departments, comparison is made with figures quoted by Szur (1957) of a series of 243 patients treated with palliative radiotherapy. In the present series and that of Szur the percentage of patients dying within one month after treatment was 19 and 13.2 respectively; between one and six months after treatment 52.5 and 60.4; between six and twelve months 16.5 and 17.8, and of those surviving one year after treatment 12 and 8.6. There is a close similarity in the two series.

Radiotherapy can be employed to diminish the effects of secondary deposits. No bony secondaries were given treatment

in this series but two patients each had a cerebral secondary deposit treated with considerable symptomatic improvement. Although one patient died six weeks after treatment was completed he was able to walk with comfort when previously he had been completely ataxic.

Radical Radiotherapy.

The purpose of radical treatment is to destroy the tumour and thereby prolong the patient's life. The following observations are concerned with patients treated by machines of what have come to be known as the "Conventional" type as opposed to the modern supervoltage machines the use of which will be described later. The dosage used varies from 4,000 to 6,000 r in a course of daily treatments spread over several weeks. This pattern of therapy was employed in 15 patients in this series, 14 men and 1 woman. Their ages ranged from 36 to 73 years. In order to withstand the strain of a radical course of treatment and to benefit from it, certain contra-indications are nowadays generally accepted. These are :-

(1) a general condition which is poor or out of proportion to a strictly localised growth,

(2) a fever not responding to antibiotics or unexplained fever which is often due to liver involvement or sepsis distal to the growth,

(3) active pulmonary tuberculosis.

Some authorities also include the following :-

(4) large tumours involving a whole lobe or lung,

(5) diffuse growth,

(6) large, rapidly recurring pleural effusion (Szur, 1957),

(7) persistent, unexplained tachycardia indicating involvement of the pericardium and/or heart,

(8) severe, persistent and unexplained thirst indicating liver involvement,

(9) oat cell growths (Levitt, 1955).

The possible benefits to be obtained from therapy are twofold. Firstly, subjective improvement in the patient's symptoms and secondly, the prolongation of his life. With regard to the first aim, careful selection of cases, modern techniques in therapy and the use of adjuvant drugs result in symptomatic improvement in the majority of cases. Garland and Sisson (1956) found it was "usually obtained" in a series of 122 cases, while Guttman (1955) reported definite symptomatic benefit in 63 out of a series of 100 patients in New York. In the present series only 2 patients were definitely worse after their treatment and improvement of varying degree occurred in the others.

With regard to the survival of treated patients opinions vary. Table 49 and Figure 7 set out the findings in the present series. In three series of patients treated with radical radiotherapy published by Guttman (1955), Smithers (1955) and Szur (1957) the percentages of patients living more than one year after treatment were 27, 37.5 and 22.4 respectively. In the present series it was 33.3.

The corresponding figures for two-year survivors were 11, 12.9 and 11.9. In the present series it was 20 but this comparatively high figure probably depends on the small number of cases concerned, only 15 cases compared with over 100 in each of the published series quoted. Watson (1956) in reporting the results of therapy at the Saskatchewan Cancer Clinic was pessimistic about the results finding them little better than those in untreated patients but the series of 151 patients started in 1932 since when methods of therapy and selection of patients have improved. Bignall (1956) in a more recent study concluded that it was unlikely that radiotherapy caused an increase of as much as 10% in the proportion of patients surviving one year and 5% in those surviving two years compared with untreated cases. Oswald (1956) considered that the 1-year survival rate after radiotherapy might be 50% and the 5-year survival about 3%. Smart and Hilton (1956), however, reported the results of treatment in 33 patients with histologically proven growths. Each was carefully selected with good general condition, a localised growth in such a position that surgery could have been undertaken with no clinical, radiographic or bronchoscopic evidence of mediastinal glandular involvement. Of those with a sufficiently long follow-up (12 cases) the 2-year survival rate was 55.6%, 3-year 38.5% and 5-year 33%.

Factors Influencing Survival.

(1) Histological type of growth. The best results are

usually obtained in squamous growths (Watson, 1956; Kutz, 1956). Undifferentiated growths are extremely radiosensitive and apparently disappear rapidly when irradiated but recurrence of the growth or appearance of previously seeded metastases vitiates the immediate improvement. Levitt voiced the opinion of others in considering the presence of an oat cell growth to be a contra-indication to treatment. In this series no conclusion can be drawn as to results for no known undifferentiated growth was treated and only one adenocarcinoma. The latter died within six months.

(2) Site of growth. This is not found to have any effect on the results of treatment (Guttman). In the present small series 1 lower lobe growth survived one year as did 2 in the main bronchi. Only 2 out of 12 in the upper lobes did so, however, but this may be due to the fact that growths in the lower lobe and main bronchi were all of the squamous variety but 8 out of the 12 upper lobe growths had no histological confirmation and might have been of those types with an inherently poorer prognosis.

(3) Age and Sex. Neither have been shown to affect results when allowances have been made for the age and sex distribution of the different histological types. In this series of six patients under the age of 60 years none survived a year after treatment, of six between 60 and 69 years three lived over a year and of three over 70 years two survived a year. The small numbers concerned and the lack of histological proof in all cases precludes any statistically valid conclusion

being drawn. The series included only one woman.

(4) Amount of irradiation. Guttman found that all his patients who survived at least eighteen months received a minimum of 5,000 r in five weeks. Smart and Hilton, however, treated the undifferentiated growths in their series with 4,000 - 4,500 r over 7 - 8 weeks with one known 5 year survivor. Squamous growths were given 5,000 - 5,500 r.

(5) The presence of metastases. The presence of these reduces the effect of treatment. Bignall found that the proportion of 1-year and 2-year survivors in those patients with mediastinal metastases present at the time of irradiation was smaller than in those without. No findings can be given in this series.

Supervoltage Radiotherapy.

Recent advances in radiotherapy include the introduction of machines capable of a potential of many million volts. The advantages of these machines such as the Linear Accelerator, the Betatron and the Cobalt Bomb are that less skin and general reactions are produced than by the less powerful conventional machines. The time for each daily treatment is reduced to only a few minutes and moreover, the patient can remain comfortably seated. Daily treatments for several weeks are given and, in lung cancer patients, the growth and the mediastinal area are irradiated. According to Morrison (1957) considerable relief of symptoms can be obtained. Results with squamous growths are as usual rather better than with

anaplastic growths because of the smaller likelihood of dissemination. For squamous growths with no mediastinal involvement 47% of his series survived 1 year and 30% for 2 years. He found in a small series of 25 patients who were considered operable but were treated by this method, the results were comparable to those obtained by surgery. Sufficiently large numbers have not yet been published to indicate whether these findings are to be expected generally. Both Watson (1956) and Ross (1957) confirm the lessened ill effects produced by supervoltage therapy. The former author, however, found his survival results not much better than those obtained by conventional machines.

Two cases only in the present series have been treated by a 4 MeV machine. Both had squamous growths and both are still alive 16 months after treatment.

Other Therapeutic Agents.

Several agents with anti-tumour activity have been employed in the treatment of inoperable lung cancers but little benefit has been obtained except in the case of radioactive isotopes in patients with malignant pleural effusions. Nitrogen Mustard gave some benefit to about half the patients treated by McAlpine (1956) but the relief was of short duration. It has the advantage however, of being available in any hospital whereas radioactive substances are not.

Radio-active Isotopes.

The most commonly used agent is radio-active gold,

Au 198 which when introduced into a pleural effusion flocculates and is deposited on the pleural surface. Its precise action is not known but it probably induces a subendothelial fibrosis with obliteration of vessels and lymphatics. The promotion of adhesions and a direct irradiation effect on the tumour are less likely actions (Andrews et al, 1953). MacKay (1957) reported benefit in about half the cases treated and Roswit (1955) obtained improvement in up to 60% of cases. The action is merely palliative. Colloidal preparations of radioactive chromium phosphate and Yttrium - 90 may be more extensively used in the future. No patients in this series received isotope therapy.

Untreated Patients.

This group consists of 180 persons. All were assessed, after diagnosis, for their fitness for surgery or radiotherapy but were rejected on the grounds of unsuitability as described in the preceeding sections (Table 43). All survival times are taken from the date of their first hospital consultation. This is shown in Life Table form in Figure 8. This indicates that within one month of that date 24% of the patients had died, within six months of it 70% had died, within twelve months 86%, within two years 96%, three years 98% and all were dead within four years. The Median Survival Time was only 2 months and the average survival time was 6.1 months. This poor survival record follows the pattern of published series. Oswald (1956) finding 41% of his patients died within 3 months of diagnosis and 76% within twelve months. Bignall (1955) found the median survival of untreated patients 9 months from the onset of symptoms while Boyd et al (1954) and Taylor and Waterhouse (1950) both found average survival times of 4 months from diagnosis and Frkovich et al (1956) 3.3 months.

Factors Influencing Survival.

(1) Histological Type. The proportion of patients in whom the histological type of growth could be determined is smaller in this group than in the surgery and radiotherapy groups as many patients were too ill to be subjected to bronchoscopy. No attempt has been made in this hospital to type the neoplastic cells found in sputum or pleural fluid so the diagnosis was established in many cases without the exact type of growth being identified. Altogether 97 patients had their growth

identified histologically and Table 50 sets out their survival. There were 38 squamous growths, 38 undifferentiated growths, 16 adenocarcinomata, 4 bronchiolar carcinomata and 1 malignant adenoma. It is evident that for the three major groups there is very little difference. The two minor groups contain only a few patients and the findings are in no way significant. Bignall (1955) found a significantly longer survival time among patients with differentiated growths than in those with undifferentiated but his analysis dated survival from the onset of symptoms and not from first hospital attendance.

(2) Age. Table 51 sets out the survival of patients above the age of 60 years. There is no very marked alteration in proportion of over 60 years to under 60 years as the survival time increases but there is a tendency for the longer living patients to include a rather higher percentage of persons over 60 years of age. This is similar to the findings of Bignall.

(3) Sex. There are 24 women among the untreated patients and Table 52 sets out the proportion in various survival groups. If the last two groups which each contain only three patients are excluded, it appears that women have a better chance of living for a year after coming to hospital than do men.

(4) Site of Tumour. There was no difference in survival pattern between those patients who had growths in the left and in the right lung or between upper and lower lobes. The series was too small for accurate analysis of the lobar

distribution.

(5) Presence of Pleural Fluid. No definite correlation can be made between the development of pleural fluid and the duration of life thereafter but of the 32 patients who already had an effusion when first seen at hospital only 5 lived longer than twelve months. Three survived between 1 and 2 years, one between 2 and 3 years and the fifth is still alive after 2 years.

(6) Duration of symptoms prior to hospital attendance. It was found by Bignall that the survival of patients after diagnosis varied with the duration of symptoms prior to diagnosis and the date of diagnosis was taken as the date of their first attendance at hospital. The worst survival record was among those with symptoms of 4 - 5 months, being rather better in those with symptoms of under 1 month and best of all among those with symptoms for over a year. Figure 9 shows the Life-Table Survival curve of four groups of untreated patients in the present series; those with symptoms of under 1 month, between 3 and 6 months, between 6 and 12 months, and over 12 months. The curves lie closely together indicating no appreciable difference in the prognosis of the groups with the exception of the fourth group, symptoms over 12 months, which is rather better than the others for the period of 6 to 12 months survival. It is, however, so little different that no significance can be attached to it and the findings in this series differ in this respect from thos of Bignall.

In spite of the fact that the average survival of

untreated patients is so poor there is a very small proportion of patients who live for several years after the presence of lung cancer has been proved beyond doubt. Two and three years survivals are not uncommon there being three of the latter in this series of 180 patients. It must be pointed out, however, that in only one was the growth proven histologically but malignant cells were found in the sputum of the second (APPENDIX, Plates 37 and 38). The third was accepted on clinical grounds. Smith (1954) reported five untreated patients whose duration of disease from the date of the first radiographic abnormality exceeded two years.

Overall Survey of Treatment and Prognosis.

As facilities for surgery and radiotherapy increased in Bedfordshire during the earlier years of this study, figures for the five years 1952 - 56 have been grouped together to show the general picture of therapy employed. In this period 194 patients with lung cancer were referred to Bedford General Hospital and Chest Clinic for diagnosis and treatment. Of these, 39 (20%) were treated by pulmonary resection and 10 (5.1%) had radical radiotherapy. Thus only a quarter of the patients were suitable for treatment likely to prolong life. Of the remaining patients, 37 (19.1%) were given palliative radiotherapy for the relief of specific symptoms and the remainding 108 (55.8%) received no treatment other than those drugs commonly prescribed for easing the patient's remaining life.

From the figures given in the preceeding sections it

is clear that, up to the present time, the treatment which holds out the greatest promise of cure is that of surgical resection and the earlier in the growth cycle of the tumour that operation can be performed the better is the chance of success. Radical radiotherapy by conventional machines is a second best form of therapy. Whether the increasing use of supervoltage machines will yield results equal to, or better than, surgery is a question for the future but it may well prove to be so. It is quite unrealistic to compare the survival curves resulting from different types of treatment and claim that they prove conclusively that surgery is the best method. Figure 10 sets out the survival curves referred to earlier, superimposed one on another. The only strictly justifiable conclusion that can be drawn from it is that those patients who were diagnosed at a stage when the growth was considered operable lived longest. Those whom, on diagnosis, were in a state when operation was impossible but were yet fit enough for radical radiotherapy lived not quite so long, and so on down the scale of treatment. The fact that those patients who were operable might have lived just as long even if they had had no operation carried out has not been disproved. The only absolute proof would be a survey of patients whose growths were considered resectable but who refused operation. As resectability can, in the end, only be ascertained when the surgeon has the lung and mediastinum in full view, a survey of such patients is unlikely ever to be made. The argument that the superiority of surgery is proved

by figures such as those of Taylor and Waterhouse who stated that the "mean duration" of disease from the first symptom was 9.9 months in non-surgical patients compared with 18.4 months in their pneumonectomy patients is not truly valid. It would only be so if the non-surgery and pneumonectomy series were composed of statistically similar patients. That series of resection and non-resection patients are in fact dissimilar in one important respect is given by Holmes Sellors' analysis which showed that there were over three times as many squamous growths and only one third as many oat cell growths in his resection cases as in a necropsy series of non-surgery cases. He stated that this greater operability of squamous growths confirmed other reports. As patients with squamous growths have, on the average, an inherently longer survival than those with oat cell growths it may be a fact that all similarly composed resection series are biased towards long survival. Although ultimate proof is lacking, the weight of present day evidence is in favour of resection as the treatment of choice. The radiotherapist must prove his case when any claim to parity is made for irradiation and this proof will be hard to come by as surgeons almost always have first pick when selection for treatment is discussed. It will take courageous, some would say almost unethical, physicians to refer apparently operable cases straight to a radiotherapist but in some centres thoracic surgeons are co-operating in this endeavour to provide a fairer test of their colleagues' therapeutic skill than

has been their lot in the past.

There is another reason why the curves in Figure 10 are not comparable, for the survival of surgery and radiotherapy cases have been estimated from the date that treatment started, that of the untreated cases has been taken from the patients' first hospital consultation. This only serves to accentuate the disparity between the treatment and non-treatment groups for if the treated patients had their survivals dated back to their first hospital consultation it would further increase their survival rates. The importance of this Figure lies not in the comparison of one curve with another, nor in its depressingly low level of curve which summarises in a few lines the meagre success of treatment over the last ten years but in the fact that it displays the likely prognosis for any new patient in this area. Providing the results of treatment do not either improve or deteriorate the outlook for such a patient can be judged from that particular curve to which his suitability for treatment places him. Price Thomas (1955) once described a lobectomy he performed for lung cancer in the presence of widespread pleural metastases. Contrary to all expectations the patient was able to lead a normal life for over five years before she died. He wrote that if one could assess the factors which enabled that person to live so long we should be well on the way to getting the key to this problem. While unexpected results such as this do occur and, therefore, caution must be exercised in forecasting the survival of any patient the prognostic index displayed in Figure 10 is a reasonable guide for the immediate future.

TABLE 40

PROPORTION OF PATIENTS SUBJECTED TO SURGERY.

Year	No. of cases.	Thoracotomies No.	%	Resections No.	%
1947	2	1	50	1	50
1948	13	1	7.7	1	7.7
1949	20	5	25	2	10
1950	32	7	21.9	4	12.5
1951	29	7	24.1	5	17.2
1952	39	13	33.3	11	28.2
1953	34	9	26.4	6	17.6
1954	37	9	24.3	5	13.5
1955	42	9	21.9	8	19.5
1956	43	12	27.9	9	20.9
Total	291	73	25.1	52	17.9

TABLE 41

TYPES OF SURGERY PERFORMED

	Wedge Resection	Lobectomy	Pneumonec-tomy
1947			1
1948			1
1949			2
1950			4
1951		1	4
1952			11
1953		2	4
1954		1	4
1955	1	1	6
1956		3	6
Total	1	8	43

FIGURE 2

TABLE 40 EXPRESSED GRAPHICALLY

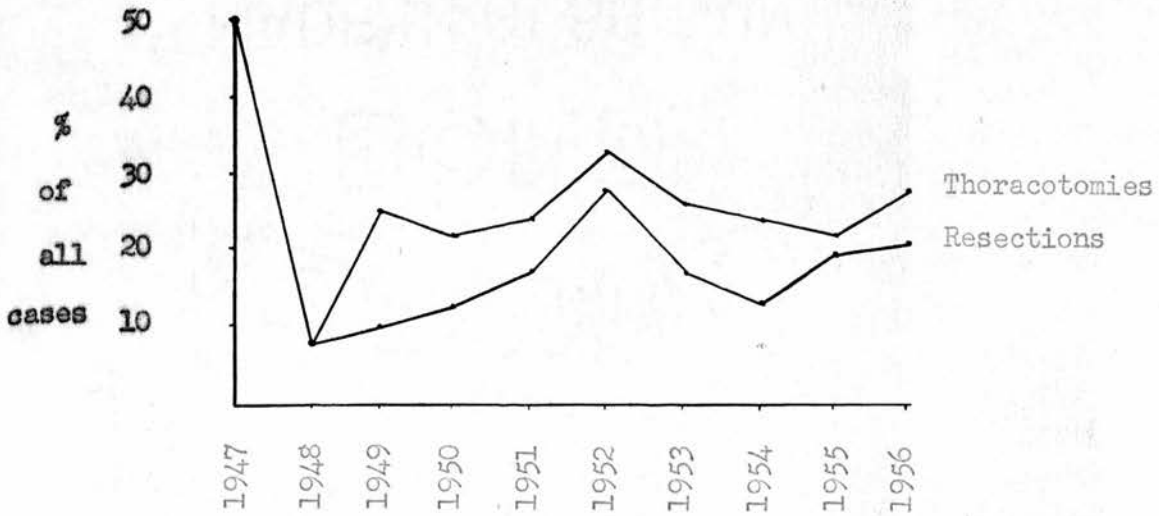


TABLE 42

THORACOTOMY, RESECTION AND SURVIVAL RATES. PRESENT SERIES AND OTHERS.

Author	Year	A No. of patients	B Exploratory Thoracotomy % of A	Resections % of A	% of B	Survivors % of all resections 3 yrs.	5 yrs.
Mason	1949	1,000	35.3	20.2	57	-	-
Taylor & Waterhouse	1950	-	-	-	-	23.9	13.7
Churchill et al.	1950	1,130	26	15	58		
Ochsner et al.	1952	948	54	35	65		19
Gibbon et al.	1953	532		30		32	22
Jones et al.	1955	704	44	23	52	28	23
Ochsner et al.	1955	644				24	21
Bignall and Moon.	1955	531					33 *
Price-Thomas.	1955	416	100	65.4			25.5
Sellors.	1955	228	100	66		30	21
Overholt and Bougas.	1956	588		34			23
Frkovich et al	1956	252	59.1	39.7	67	22.4	16.3
Smith.	1957	147	97.2		97.2		
Nicholson et al.	1957	720	35	18.3	42	33.3	
Gifford and Waddington.	1957	2,156	33	21	63		28 *
Present series.		291	25.1	17.9	71	22	11

* Excludes deaths within two months of operation.

FIGURE 3

LIFE TABLE SURVIVAL CURVE OF ALL RESECTION CASES.

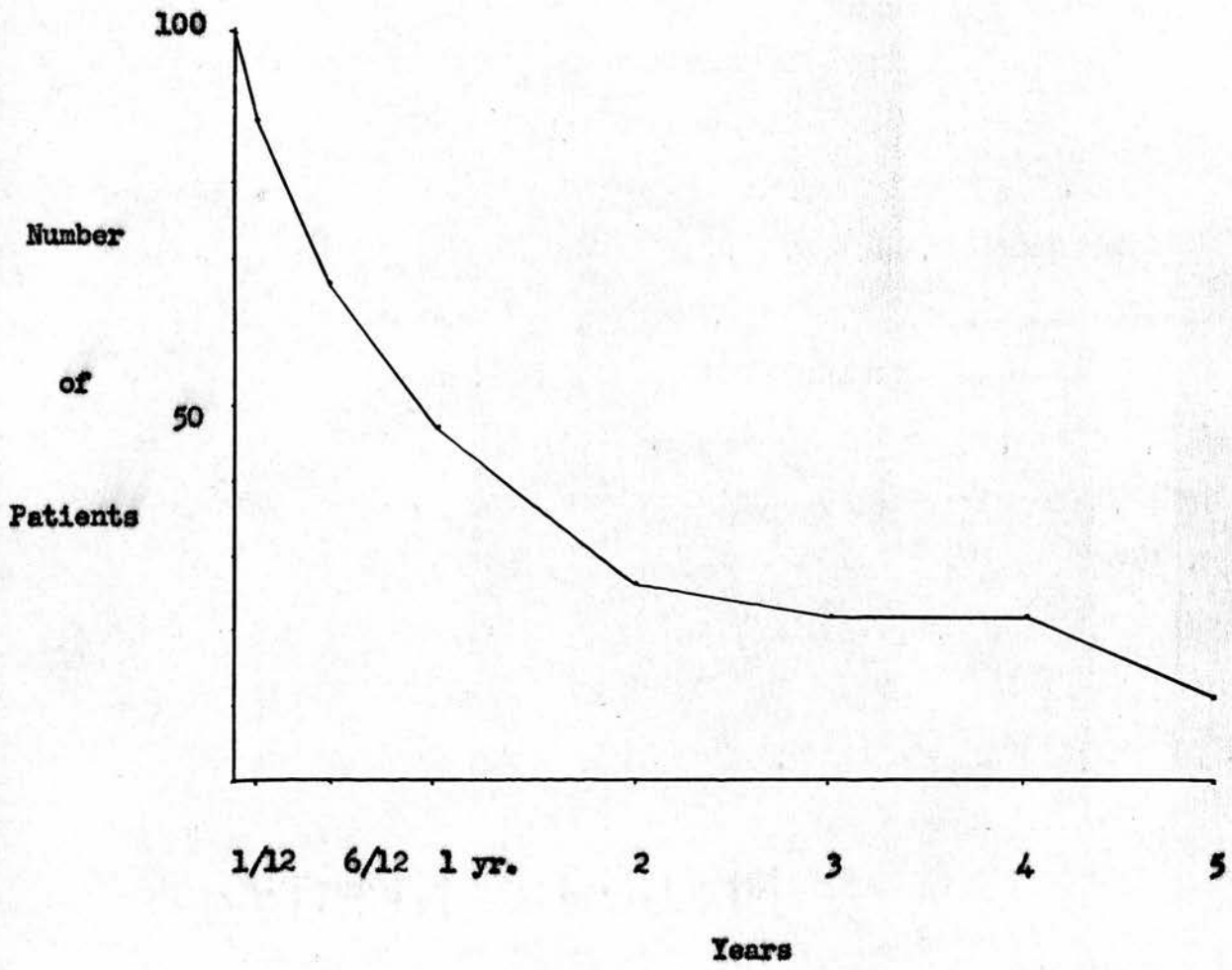


TABLE 43

CRITERIA OF NON-RESECTABILITY.

Reason	Number of Cases	%
General condition too poor and/or poor pulmonary reserve.	75	31.5
Bronchoscopically inoperable	30	12.6
Extrathoracic spread	57	23.9
Refused operation	19	8.0
S.V.C. Obstruction	9	3.7
Diagnosed at Post Mortem	9	3.7
Phrenic Nerve Paralysis	7	3.0
Malignant Pleural Effusion	6	2.4
Laryngeal Nerve Paralysis	4	1.6
Secondary in opposite lung	1	0.4
Chest wall involved	1	0.4
Mediastinal involvement too extensive at thoracotomy	21	8.8

TABLE 44

POST-OPERATIVE MORTALITY RATES. PRESENT SERIES AND OTHERS.

Author	Year	"Post-Operative" period in months	Years	Mortality Rate as percentage of resections
Churchill et al	1950	-	1933 - 47 1948 - 49	(a) 28.7 (b) 22.6 * (a) 3.7 (b) 3.8
Ochsner et al	1952	"Hospital Mortality"	1940 - 46 1947 - 51	20 17
Taylor and Waterhouse	1950	1	1939 - 40 1947 - 48	33 15
Ehler et al	1954	1	1937 - 49 1950 - 51	17.8 7.1
Bignall and Moon	1955	2	1940 - 46 1947 - 49 1950 - 51	19 16 10
Sellors	1955	4	1940 - 48 1949 - 50	24 9
Gifford and Waddington	1957	2	before 1948 1949 - 54	31 21.5
Present series		1	1947 - 51 1952 - 56	15.3 12.8

* (a) = pneumonectomies, (b) = lobectomies.

TABLE 45

2-YEAR SURVIVAL RATE OF RESECTION CASES BY DURATION OF SYMPTOMS.

Duration of Symptoms. Months.	No. of cases.	2-year Survivors.	Survival Rate. %	Proportion of Squamous growths. %
Under 6	23	6	26	56
6 - 9	9	1	11	70
Over 9	11	3	27.3	90

TABLE 46

SURVIVAL RATES OF PATIENTS WITH AND WITHOUT REGIONAL GLAND INVASION AT THE TIME OF OPERATION. PRESENT SERIES AND OTHERS.

Author	Year of publication.	Follow-up period in years.	% of patients alive at end of follow-up period. glands involved.	glands not involved.
Carlisle et al	1951	5	25	63.2
Ochsner et al	1952	5	10	38
Aufses	1953	4	6	30
Ehler et al	1954	5	0	
Bignall and Moon	1955	(2	27	61
		(5	11	48
Toft	1955	3	0	
Price-Thomas	1955	5	5.5	32.9
Belcher	1956	(2	35	55
		(5	20	77
Frkovich et al	1956	3	0	48.3
Present Series		3	5	52

FIGURE 4

LIFE TABLE SURVIVAL CURVE OF ALL RESECTION CASES.

A WITH NO INVOLVEMENT OF REGIONAL GLANDS.
B WITH INVOLVEMENT OF REGIONAL GLANDS.

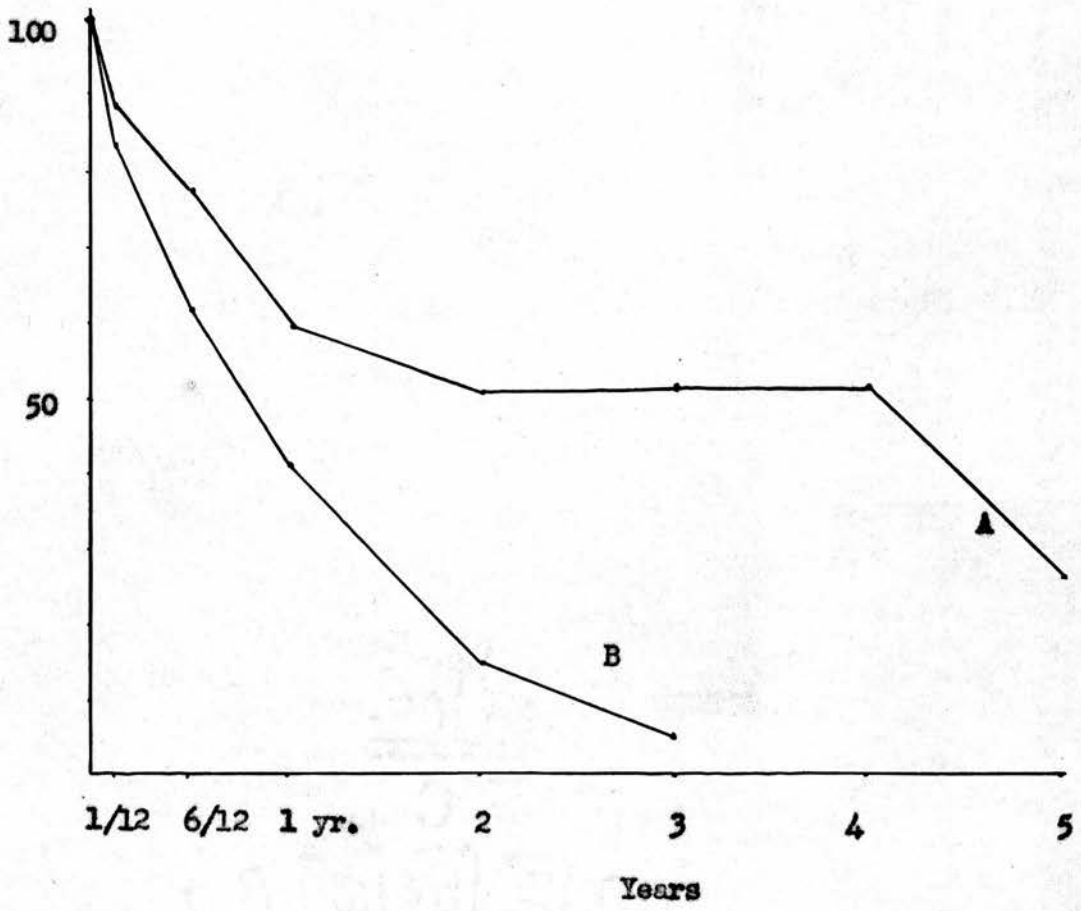


TABLE 47

SURVIVAL AND HISTOLOGICAL TYPE OF GROWTH IN ALL PATIENTS RECEIVING RADIOTHERAPY.

Survival in Months	Total	Squamous	Undiff.	Adenoca.	Malig. Aden.	Unknown
Under 1	8	4				4
1 - 6	29	7	4	1	1	16
6 - 12	10	2	2 *			6
12 - 24	8	5 +		1		2
24 - 36	4	4 *				

\+ 4 patients still alive

* 1 patient still alive

FIGURE 5

LIFE TABLE SURVIVAL CURVE OF ABOVE PATIENTS.

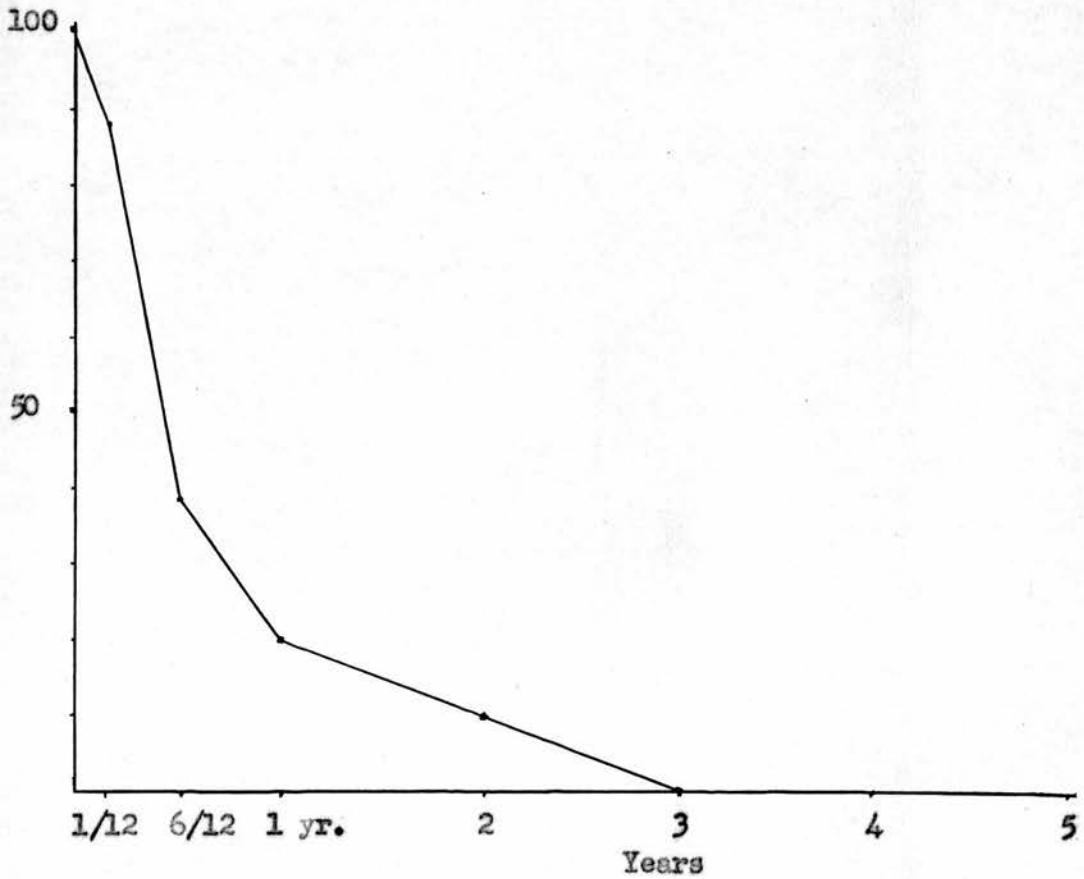


TABLE 48

SURVIVAL AND HISTOLOGICAL TYPE OF GROWTH IN PATIENTS RECEIVING PALLIATIVE RADIOTHERAPY.

Survival in Months	Total	Squamous	Undiff.	Adenoca.	Malig.Aden.	Unknown
Under 1	8	4				4
1 - 6	22	6	4		1	11
6 - 12	7	1	2 *			4
12 - 24	4	2 +		1		1
24 - 36	1	1				

* 1 patient still alive
\+ Both patients still alive

FIGURE 6

LIFE TABLE SURVIVAL CURVE OF ABOVE PATIENTS.

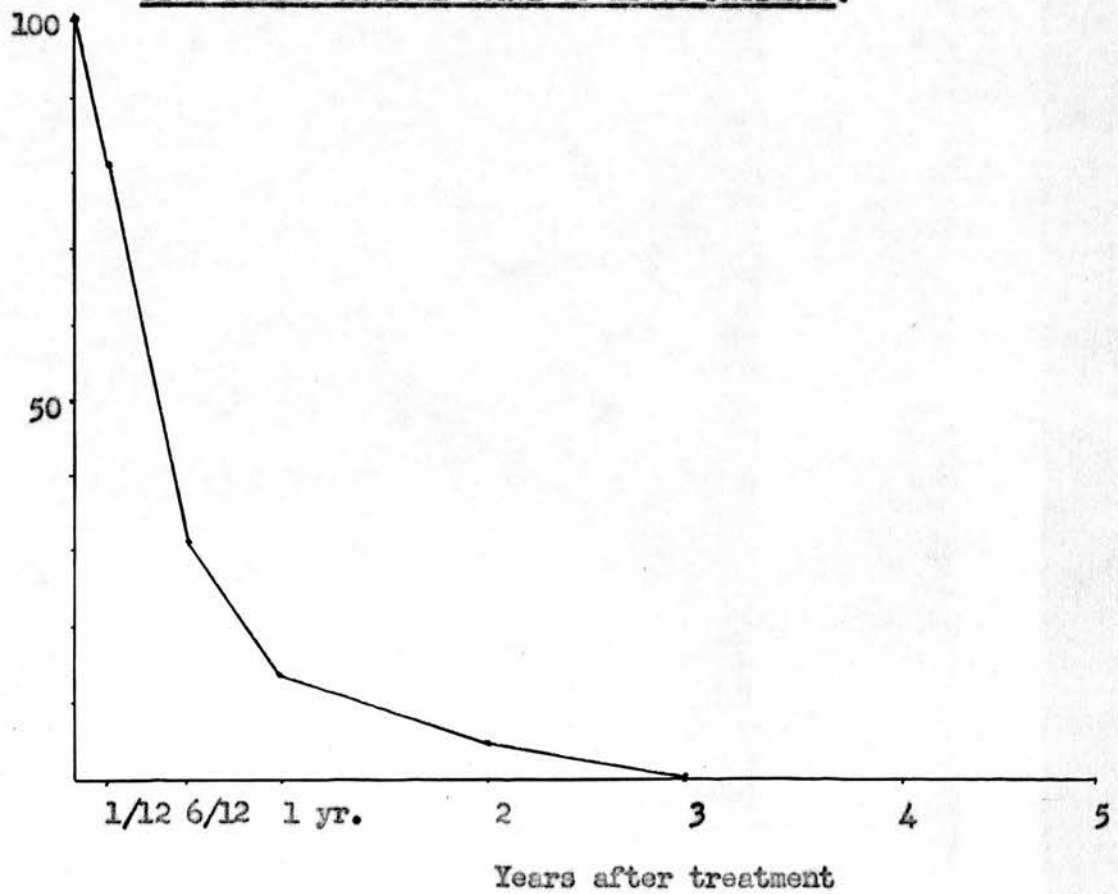


TABLE 49

SURVIVAL AND HISTOLOGICAL TYPE OF GROWTH IN PATIENTS RECEIVING RADICAL RADIOTHERAPY.

Survival in Months	Total	Histological Type			
		Squamous	Undiff.	Adenoca.	Unknown
Under 1	7	1		1	5
1 - 6	3	1			2
12 - 24	2	1			1
24 - 36	3	3 *			

* 1 patient still alive

FIGURE 7

LIFE TABLE SURVIVAL CURVE OF ABOVE PATIENTS.

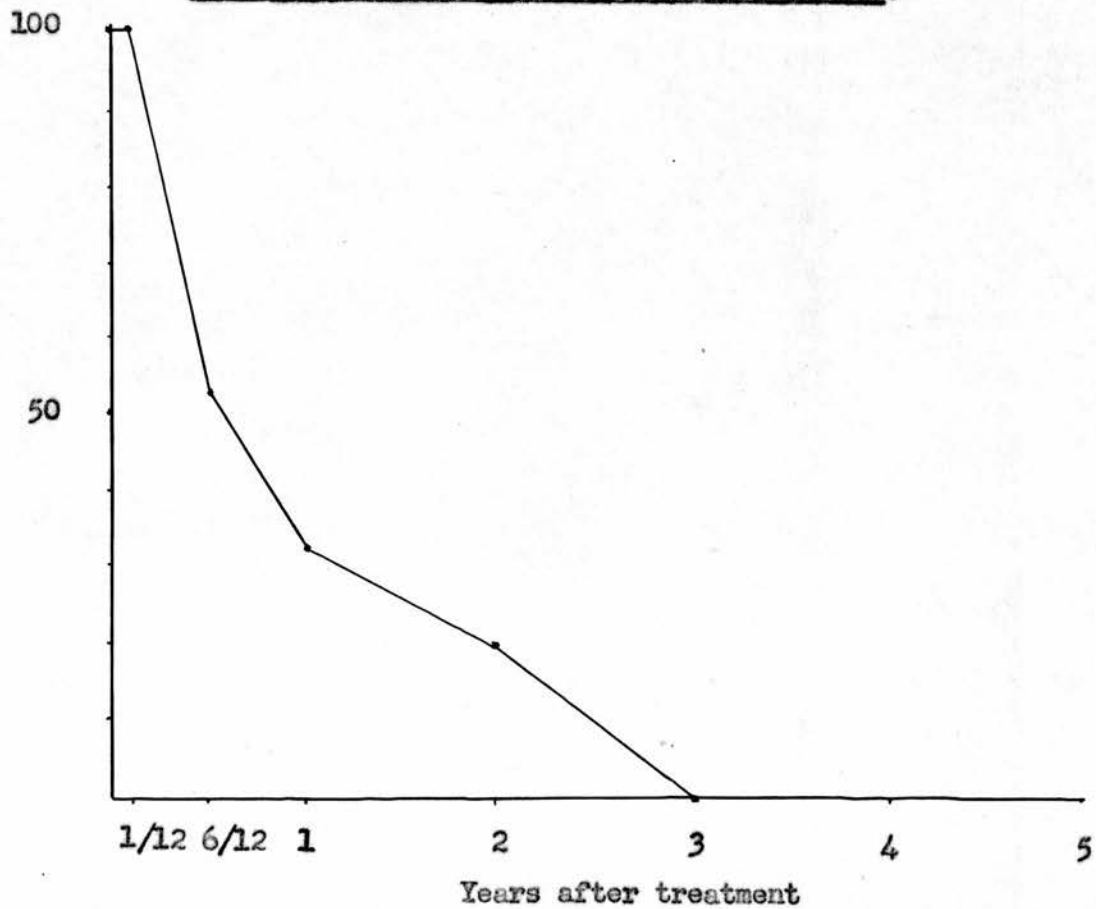


FIGURE 8

LIFE TABLE SURVIVAL CURVE OF UNTREATED PATIENTS.

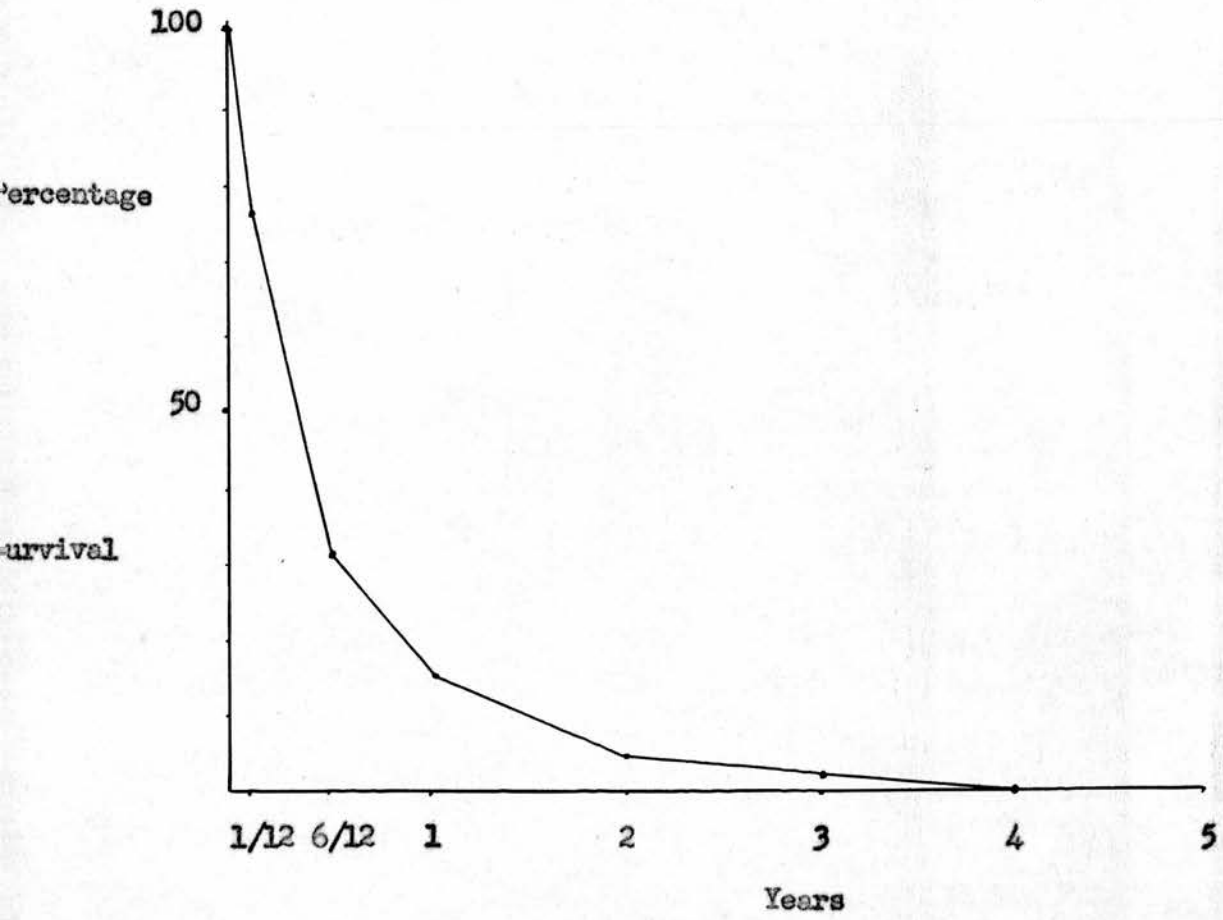


TABLE 50

SURVIVAL OF UNTREATED PATIENTS BY HISTOLOGICAL TYPE OF GROWTH.

Histological Type	Percentage of each type dead within		
	1 month	Six months	1 year
Squamous	23.6	76.4	95
Undifferentiated	34.2	81.7	95
Adenocarcinoma	37.5	75	88
Bronchiolar Car.	25	75	75
Malignant Adenoma	100		

TABLE 51

SURVIVAL OF UNTREATED PATIENTS OVER AND UNDER 60 YEARS OF AGE.

	Patients dying within						Total
	1 month	1 - 6 months	6-12 months	1-2 yrs.	2-3 yrs.	3-4 yrs.	
Number of patients of all ages.	43	84	28	19	3	3	180
Number of patients over 60 years.	26	47	17	10	2	3	105
Percentage over 60 years.	60	56	60	52	66	100	58

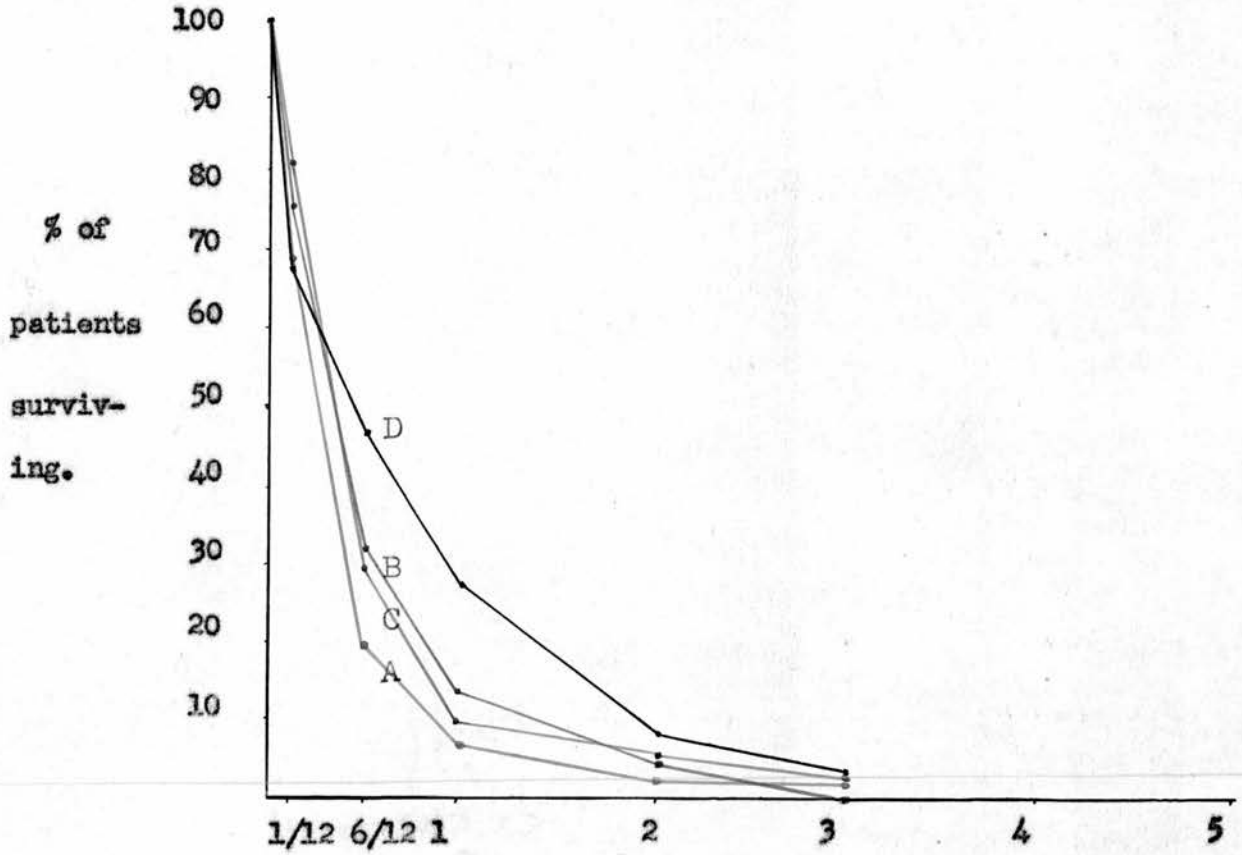
TABLE 52

SURVIVAL OF UNTREATED PATIENTS BY SEX.

	Patients dying within						Total
	1 month	1 - 6 months	6-12 months	1-2 yrs.	2-3 yrs.	3-4 yrs.	
Number of patients of both sexes.	43	84	28	19	3	3	180
Number of women	5	10	4	5	0	0	24
Percentage of women in series.	11.6	12	14.2	26.3	0	0	13.3

FIGURE 9

SURVIVAL OF UNTREATED PATIENTS BY DURATION OF SYMPTOMS.



Survival in Years after first hospital attendance.

Survival in months after first hospital attendance.

A = Those Patients with symptoms lasting under 1 month prior to first hospital attendance.

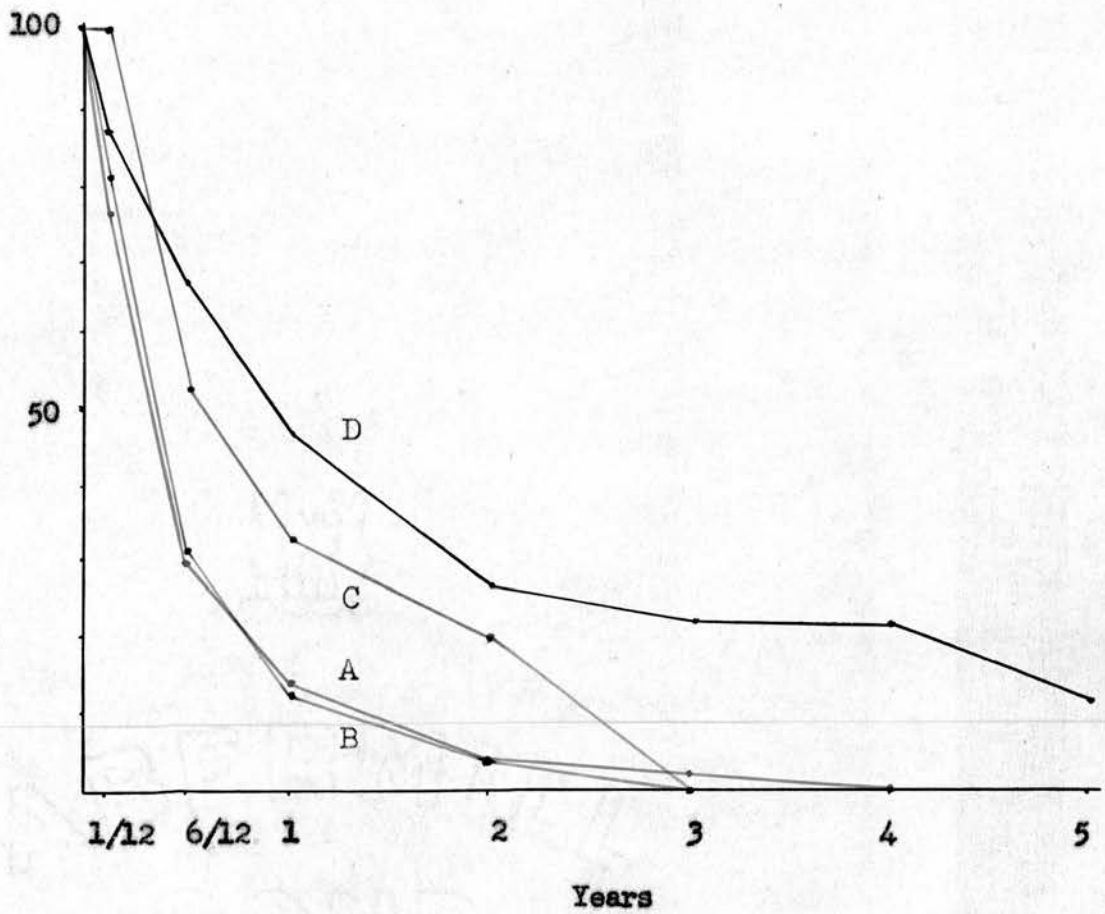
B = Those Patients with symptoms lasting between 3 and 6 months prior to first hospital attendance.

C = Those Patients with symptoms lasting between 6 and 12 months prior to first hospital attendance.

D = Those Patients with symptoms lasting over 12 months prior to first hospital attendance.

FIGURE 10

LIFE TABLE SURVIVAL CURVE OF ALL PATIENTS IN SERIES.



A = Patients with No treatment.
B = Patients treated with Palliative Radiotherapy.
C = Patients treated with Radical Radiotherapy.
D = Patients treated with Resection

SUMMARY AND CONCLUSIONS

This thesis has been concerned primarily with the analysis of the case records of 291 persons suffering from lung cancer and comparing the findings with published works. It has also dealt with the incidence of this condition in a prescribed area and in broad outline with its aetiology. There follows a recapitulation of the more important facts elicited.

(1) The incidence of bronchial carcinoma is higher in Great Britain than in any other country in which statistics are available. It has increased over the past half century and, in the main, continues to do so. The increase is greater in men than women and greater in urban areas than in rural. Some, possibly a considerable proportion, of this rise has been due to improved diagnosis, an ageing population, and other factors, but there has been a definite and alarming real increase in incidence during the twentieth century.

(2) In the prescribed survey area of North Bedfordshire the incidence of bronchial carcinoma during the years 1950 to 1956 was seen to be in accord with the national figures, taking into account the largely rural nature of the area. The increase in incidence from 1950 to 1956 was in close accord with the

national increase.

(3) An annual average of three quarters of the lung cancer patients in the area from 1947 to 1956 were seen at, if not treated in, Bedford General Hospital and Chest Clinic and the series of 291 patients gave a fair sample of the disease in this area.

(4) No specific cause for lung cancer has been identified. The incidence of the disease is higher than average among persons exposed to particular substances, which include arsenic and certain hydrocarbons derived from the combustion of coal and tobacco. There is no universal agreement as to relative importance of these and other possible factors, but a wide body of responsible opinion believes that the major factors concerned are the inhalation of tobacco and industrial smoke, in that order of importance. Considerable statistical evidence supports this contention but direct experimental proof has not been obtained. A proportion of cases may originate in lung scars but it has not been claimed that this is a major source of cases as it fails to account for sex and geographical differences in incidence.

In the present series, the findings with regard to tobacco smoking were, in the main, similar to national figures. No higher incidence was noted in a portion of the survey area which was more contaminated by industrial smoke than the remainder.

(5) There is a wide variety of terms used to describe

the histology of bronchial carcinoma, but if a broad classification is used, cases occur in the approximate proportion of squamous growths 50%, undifferentiated growths 30%, adenocarcinomata 15%, and minor varieties from 0 - 5%. This was so in the present series. The differing pathological and clinical features of each type have been surveyed. Findings in this series confirmed the fact that squamous growths are usually slower growing, remain localised for longer, are more often resectable, and have a better prognosis than other varieties. Undifferentiated and adenocarcinomatous growths are equally malignant, both metastasing relatively early, and therefore frequently inoperable. The reported tendency of adenocarcinomata to be peripheral in situation was confirmed.

(6) The highest resection rates were among those patients who were picked-up before symptoms developed, and were lowest among those referred for consultation because of extra-thoracic symptoms. Thus, almost two-thirds of the patients picked up by M.M.R. were suitable for resection and one-third of those referred to a Miniature film session held in the chest clinic to which patients could be referred directly by their practitioner without hospital consultation, but only 6.5% of patients referred to departments of the hospital other than the chest clinic. This latter group had the longest period of symptoms.

It could be concluded that the greatest hope for the future with regard to early treatment lay in the use of M.M.R. and mini-film sessions which the public might attend with the

minimum of delay and inconvenience. The employment of M.M.R. on a nation-wide basis shows a poor return for the time and labour employed unless some means can be devised for limiting the attendance to the population at greatest risk, men of middle age and over.

In spite of increased awareness of the disease among the public and general practitioners, there has been little improvement over ten years in the duration of symptoms before patients were referred to hospital. The time required for diagnosis has shortened and reasons for this have been given. The average time required in this hospital bears favourable comparison with figures quoted from other sources and the claim that chest clinics are a source of delay in the patients' obtaining surgical treatment has been refuted. Over four-fifths of the patients were diagnosed and treatment arranged within two months of coming to hospital; in the last year of the survey this applied to more than nine patients out of ten.

(7) The incidence of symptoms and physical signs found in this series of patients were in accord with other publications. No attempt was made to assess the prognostic significance of individual symptoms with the exception of haemoptysis which was considered in some detail. It was commoner with squamous and bronchiolar growths than the other varieties. The reported association between hypertrophic arthropathy and peripheral lung cancers was confirmed although finger clubbing was not so related. The report that arthropathy does not occur with oat-celled

growths was not confirmed. The association of lung cancer and pulmonary tuberculosis has been briefly reviewed. The development of a diaphragmatic paralysis should be added to those features occurring in a patient with pulmonary tuberculosis which have been reported as being suspicious of a possible concomitant growth.

(8) The fact that the vast majority of persons with lung cancer who have developed symptoms sufficient to warrant hospital consultation are found to have abnormal radiographs was confirmed. The opposite, radiographic abnormality without symptoms, is more common and 13 asymptomatic cases were included in the series. The importance of a circumscribed peripheral shadow or an enlarged hilum in these cases was noted. In general, the radiographic features were in accord with published findings. The results of fluoroscopy, tomography and bronchography have been analysed and their value in diagnosis stressed. The greatest difficulty in differential diagnosis lay in those patients presenting with slowly resolving pneumonias, or with 'coin lesions', and in those with concomitant pulmonary tuberculosis.

(9) Although bronchoscopy could be carried out in only just over half the patients, evidence of growth was obtained in nearly 80% of these cases, a figure higher than in most published work. It was shown that if there were grounds for exploratory thoracotomy, failure to demonstrate the growth bronchoscopically should never prevent the operation. Regional glands were involved much less frequently when the cancer was not seen by bronchoscopy than when it was.

Exfoliative cytology was found to be a useful investigation in this area, just over one half of the patients submitting specimens being proved to have growths by this means. This figure is lower than several reported elsewhere, but the failure to obtain a higher rate was largely due to the failure to submit a sufficient number of specimens per patient. It was considered, on analysis, that three sputum specimens per patient was the optimum number for maximum success tempered by practical limitations of the pathologist's time. The greatest value of the procedure probably lay in the diagnosis of growths beyond bronchoscopic vision, 50% of these being confirmed by cytology. Other more minor diagnostic procedures have been reviewed.

(10) An increasing number of cases throughout the ten year period have been submitted for surgical treatment. From a review of the literature it was found that between one and two thirds of lung cancer patients are suitable for exploratory thoracotomy and about one quarter for resection. The majority of these reports emanate from surgical centres and therefore give an optimistic picture and the proportion of such cases in the present series, 25.1% and 17.9% gives a more accurate estimation of the situation as it affects patients referred to a general hospital. The resectability rate for the second five years of the survey was 20% and it is unlikely that, in the absence of any major advance in earlier diagnosis, this figure will rise much further than 25%. One possible advance is an increase in the number of cases diagnosed by all forms of miniature radiography and

these cases have a relatively high resectability rate in most published series, although all authorities do not agree. The rate was 62,5% in the present series, but numbers were few.

(11) Analysis of survival rates indicated that to base conclusions on a three-year follow-up was almost as acceptable as on five-years. Two years was insufficiently reliable. The average three and five-year survival rates among the published works quoted were 28% and 23% respectively. In this series they were 22% and 11% although the latter figure might be 19% with a few more months' follow-up. Factors influencing survival after resection were found, in the main, to coincide with published work, the most important being involvement or otherwise of regional lymph nodes. Other factors with influence were the duration of symptoms and involvement of the chest wall. The site of growth, age per se, sex, and extent of operation did not influence results. Contrary to most publications squamous growths had a poor prognosis. This could be attributed to the small number of such cases for analysis and the presence of the more important factor of regional node involvement.

(12) The results of radical radiotherapy were poor by comparison with surgery. Hope has been expressed that supervoltage machines may give more comparable results, as they have done already in a limited number of cases elsewhere. The value of palliative radiotherapy in relieving certain specified symptoms was confirmed. Of those patients receiving no treatment likely to prolong life, the type and site of growth, duration of symptoms, and sex had little

effect on duration of life. The survival of untreated women was better than men. The fallacies inherent in the comparison of results obtained from different methods of treatment has been discussed.

(13) The main object of this thesis was to demonstrate the natural incidence of lung cancer in a geographical area and to study the means by which its victims came to diagnosis and treatment, and the scope of that treatment. There have been few publications of this type, the majority have emanated from specialised departments involving a degree of selection of patients. The survey has shown that the findings in this area are substantially the same as those based on national figures. As this is not true of some other diseases such as tuberculosis, some importance, even if negative, is attached to the results. A second purpose of the work has been to demonstrate the gradual development over ten years of diagnostic accuracy and therapeutic achievement. Although treatment in most patients is still unsatisfactory an organisation has been built up between general practitioner, hospital physician and thoracic surgeon which is essential for even the limited success of the present and which will be able to take advantage of any future developments in treatment.

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BIBLIOGRAPHY.

Agricola, G. (1556). De re metallica. E Konig, Basle.

Aird, I., Bentall, H.H., Mehigan, J.A., and Roberts, J.A.F. (1954). Brit. med. J., 2, 315.

Anderson, H.J., and Pierce, J.W. (1954). Thorax, 9, 100.

Andrews, G.A., Root, S.W., and Kniseley, R.M. (1953). Cancer, 6, 294.

Auerbach, O., Gere, J.B., Forman, J.B., Petrick, T.G., Smetlin, H.J., Muesam, G.E., Kassouny, D.Y., and Stout, A.P. (1957). New Engl. J. Med., 256, 97.

Aufses, A.H. (1953). J. Mt. Sinai Hosp., 20, 212.

_____ (1954). J. thorac. Surg., 28, 392.

Bailey, E.J., Kennaway, E.L., and Urquhart, M.E. (1956). Brit. J. Cancer, 11, 49.

Barth, L., and Kiessling, J. (1956). Z. Laryng. Rhinol., 35, 429.

Belcher, J.R. (1956). Lancet, 1, 349.

Belsey, R.H.R., and Valentine, J.C. (1951). J. Path. Bact., 63, 377.

Berkson, J. (1955). Proc. Mayo. Clin., 30, 319.

Bidstrup, P.L., and Case, R.A.M. (1956). Brit. J. industr. Med., 13. 260.

Bignall, J.R. (1955). Lancet, 2, 210.

_____ (1956). Ibid, 1, 876.

_____ and Moon, A.J. (1955). Thorax, 10, 183.

Blakemore, F., Bosworth, T.J., and Green, H.N. (1948). J. Comp. Path., 58, 267.

Blanshard, G. (1955). Lancet, 2, 897.

Bondi, G., and Leits, V. (1952). New Engl. J. Med., 247, 506.

Bonser, G.M., Faulds, J.S., and Stewart, M.J. (1955). Amer. J. Clin. Path., 25, 126.

Boucot, K.R., and Sokoloff, M.J. (1955). Dis. Chest, 27, 369.

Boyd, D.P., Smedal, M.I., Kirtland, H.B., Kelley, G.E., and Trump, J.G. (1954). J.thorac. Surg., 28, 392.

Boyland, E., Gasson, J.E., and Williams, D.C. (1956). Lancet, 2, 975.

Brain, W.R. (1957). Tubercle, Lond., 38, 225.

Brea, M.M. (1948). Year Book of General Surgery. Year Book Publishers, Chicago.

Brett, G.Z., Benjamin, B., Craig, J.W., and Freeman, V. (1956). Brit. med. J., 1, 719.

Brocard, H., Choffel, C., Bouvier, M., Solignac, P., and Ledu, M. (1954). Bull. Soc. Méd. Hôp. Paris, 70, 447.

Brock, R.C. (1948). Guy's Hosp. Rep., 97, 75.

_____ and Whytehead, L.L. (1955). Brit. J. Surg., 43, 8.

Bromley, L.L., and Szur, L. (1955). Lancet, 2, 937.

Brooks, W.D.W., Davidson, M., Thomas, P.C., Robson, K., and Smithers, D.W. (1951). Thorax, 6, 1.

Brown, D.E.M. (1952). Brit. J. Radiol., 25, 472.

Bryson, C.C., and Spencer, H. (1951). Quart. J. Med., 20, 173.

Buffmire, D.K., and McDonald, J.R. (1951). Surg. Clin. N. Amer., 31, 1191.

Cahan, W.G., and Farr, H.W. (1950). Cancer, 3, 475.

Carlisle, J.C., McDonald, J.R., and Harrington, S.W. (1951). J. thorac. Surg., 22, 74.

Cheraton, F.B., and Brierley, J.B. (1957). Brit. med. J., 1, 765.

Churchill, E., Sweet, R., Soutter, L., and Scannell, J. (1950). J. thorac. Surg., 20, 349.

Clemmesen, J., and Busk, T. (1947). Brit. J. Cancer, 1, 253.

_____ Nielson, A., and Jensen, E. (1953). Acta Un. int. Cancr., 9, 603.

Clerf, L.H., and Herbut, P.A. (1950). Amer. Rev. Tuberc., 61, 60.

_____ (1952). J. Amer. med. Ass., 150, 793.

Commins, B.T., Waller, R.E., and Lawther, P.J. (1956). Brit. med. J., 2, 753.

Cook, J.W. (1957). Ibid, 2, 696.

Cooper, R.L. (1954). Analyst, 79, 573.

_____ Lindsay, A., and Waller, R. (1954) Chem. and Industr., 1419.

Craig, J.W. (1937). Brit. med. J., 1, 750.

Craver, L.F., and Binkley, J.S. (1939). J.thorac. Surg., 8, 436.

Cudkowicz, L., and Armstrong, J.B. (1953). Thorax, 8, 152.

_____ and Wraith, D.G. (1957). Brit. J. Tuberc., 51, 14.

Cureton, R.J., and Hill, I.M. (1955). Thorax, 10, 131.

Daff, M.E., Doll, R., and Kennaway, E.L. (1951). Brit. J. Cancer, 5, 1.

Daniels, A.C. (1949). Dis. Chest, 16, 360.

Davidson, M., Smithers, D.W., and Tubbs, O.S. (1951). The Diagnosis and Treatment of Intrathoracic New Growths. Oxford University Press, London.

Decker, H.R. (1955) J. thorac. Surg., 30, 230.

Delarue, J. (1955). Schweiz. Z. Path., 18, 820.

Denk, W. (1953). Beitr. Klin. Chir., 186, 282.

Denny Brown, D. (1948). J.Neurol. Psychopath., 11, 73.

Doll, R. (1953). Brit. med. J., 2, 521.

_____ (1955). Brit. J. industr. Med., 12, 81.

_____ and Hill, A.B. (1950). Brit. med. J. 2, 739.

_____ (1954). Ibid, 1, 1451.

_____ (1956). Ibid, 2, 1071.

_____ and Kreyberg, L., (1957). Brit. J. Cancer, 11, 43.

Dorn, H.F. (1953). Acta Un. int. cancr., 9, 552.

Dotter, G., and Steinberg, L. (1951). Ann. Roentgenol., 20, 238.

Dudgeon, L.S., and Wrigley, C.H. (1935). J.Laryng., 50, 752.

Dungal, N. (1950). Lancet, 2, 245.

Dutra, F.R., and Geraci, C.L. (1954). J. Amer. med. Ass., 155, 21.

Edwards, A.T. (1946). Thorax, 1, 1.

Ehler, A., Strannahan, A., and Olson, K.B. (1954). New Engl. J. Med., 251, 207.

Ellman, P. (1953). Proc. R. Soc. Med., 46, 851.

Epstein, I.S., and Sevag, M.G. (1956). Cancer, 9, 1075.

Evans, R.W. (1956). Histological Appearance of Tumours. E.S.Livingstone, Edinburgh.

Falk, H.L., Markul, I., and Kotin, P. (1956). Arch. industr. Hyg., 13, 13.

Fisher, R.A. (1957). Brit. med. J., 2, 297.

Flavell, G. (1956). Lancet, 1, 260.

Forster, E., Sichel, Z., and Roegel, E. (1954). J. thorac. Surg., 27, 593.

Foot, N.C. (1955). Amer. J. clin. Path., 25, 223.

Frain, C., Even, R., Roujeau, J., Marlois , and Talamas, (1955). J. Radiol. Electrol. 36, 154.

Frkovich, G., Robertson, R., and Gourlay, R. (1956). Canad. Med. Ass. J., 75, 1207.

Gall, E.A., Bennett, G.A., and Bauer, W. (1951). Amer. J. Path., 27, 349.

Galluzzi, S., and Payne, P.M. (1956). Brit. J. Cancer, 10, 408.

Garland, L.H. (1955). Amer. J. Roentgenol., 74, 402.

———— and Sisson, M.A. (1956). Radiology, 67, 48.

Geddes, J.E. (1957). Personal communication.

Geever, E.F., Neubuerger, K.T., and Davis, C.L. (1943). Amer. J. Path., 19, 913.

Gelzer, J. (1956). Virchows Arch., 329, 504.

Gibbon, J., Allbritten, F., Templeton, J., and Nealton, T. Jr. (1953). Ann. Surg., 138, 489.

Gifford, J.H., and Waddington, J.K.B. (1957). Brit. med. J., 3, 723.

Gould, D.M. (1945). J.Amer. med. Ass., 127, 753.

Goulden, F., and Tipler, M.M. (1949). Brit. J. Cancer, 3, 157.

Gowan, G., and Frank, B. (1952). Ann. intern. Med., 36, 138.

Graham, E.A., and Singer, J.J. (1933). J. Amer. med. Ass., 101, 1371.

———— Wynder, E.L., and Croninger, A.B. (1952). Science, 116, 521.

Gray's Anatomy (1948). Edited by Johnston, T.B., and Willis, J. 31st Ed. Longmans. Green ind. Co., London.

Green, H.N. (1954). Brit. med. J., 2, 1374.

———— Wakefield, J., and Littlewood, G. (1957). Brit. med. J., 2, 779.

Green, H.W. (1926). Amer. J. publ. Hlth., 16, 605.

Greenberg, R.A. (1956). Conn. St. med. J., 20, 857.

Gronqvist, Y.K.J., Clagett, O.T., and McDonald, J.R. (1957). J. thorac. Surg., 33, 487.

Guiss, L.W. (1955). Cancer, 8, 219.

Guttman, R.J. (1955). Ibid, 8, 1254.

Haerting, F.H., and Hesse, W. (1876). Vischr. gerichtl. Med., 30, 296.

Hammond, E.C., and Horn, D. (1954). J. Amer. med. Ass., 155, 1316.

Hampeln, P. (1897). Z. clin. Med., 32, 247.

Hanbury, W.J., Cureton, R.J.R., and Simon, G. (1954). Thorax, 9, 304.

———— and Hill, I.M. (1956). Ibid, 11, 135.

Hart, P.L. de V. (1954). Brit. med. J., 1, 606.

Helm, W., and Moon, A. (1952). Brit. J. Tuberc., 46, 87.

Herbut, P.A. (1946a). Amer. J. Path., 20, 911.

———— (1946b). Arch. Path. (Lab. Med.), 41, 175

———— (1956). Ann. N.Y. Acad. Sci., 63, 1374.

Hilding, A.C. (1957). Trans. Amer. Acad. Opthal. Oto-laryng., 61, 69.

Hill, A.B., and Faning, E.L. (1948). Brit. J. industr. Med., 5, 1.

Hippocrates (1923). Works. Loeb Classical Library. Heineman, London.

Holman, R.A. (1957). Brit. med. J., 2, 881.

Hueper, W.C. (1955). A Quest into the Environmental causes of Cancer of the Lung. Public Health Monograph No. 36, United States Government Printing Office, Washington.

Huiginga, E. (1952). J. thorac. Surg., 23, 445.

Hutchison, H.E. (1952). Cancer, 5, 884.

Isaacson, N.H., and Rapoport, P. (1946). Ann. intern. Med., 25, 893.

Jack, G.D. (1952). Trans. med. - chir. Soc. Edinb., 132, 75.

Jackson, E., Bertoli, F., and Ackerman, L.V. (1951). J. thorac. Surg., 21, 7.

James, W.R. (1955). Brit. J. industr. Med., 12, 87.

Jennings, R.C., and Shaw, K.M. (1953). Thorax, 8, 288.

Jones, J.C., Robinson, J.L., and Meyer, B.W. (1955). Arch. Surg., Chicago, 70, 265.

Kennaway, E.L. (1953). Brit. J. Cancer, 5, 153.

———— and Kennaway, N.M. (1947a). Ibid, 1, 253.

———————————— (1947b). Ibid, 1, 260.

Kirklin, J.W., McDonald, J.R., Clagett, O.T., Moersch, H.J., and Gage, R.P. (1955). Surg. Gynae. Obstr., 100, 429.

Korteweg, R. (1953). Acta Un. int. Cancr., 9, 589.

Kotin, P., Falk, H.L., and Thomas, M. (1955). Arch. industr. Hyg., 11, 113.

Kraus, A.S. (1954). Publ. Hlth. Rep., Wash., 69, 1211.

———— Strnad, F., and Ehbrecht, A. (1954). Med. Mschr., Stuttgart, 4, 225.

Kreyberg, L. (1954). Brit. J. Cancer., 8, 199.

———— (1955). Ibid, 9, 495.

Kutz, E.R. (1956). J. thorac. Surg., 32, 165.

Lea, A.J. (1952). Thorax, 7, 305.

Lennox, B., and Prichard, S. (1950). Quart. J. Med., 19, 97.

Levitt, W.M. (1955). Brit. J. Tuberc, 49, 260.

Liebow, A.A. (1951). Atlas of Tumour Pathology. Armed Forces Institute of Pathology, Washington.

Liebow, A., Lindskog, G., and Bloomer, W. (1948). Cancer, 1, 223.

Lindskog, G.E. (1946). Ann. Surg., 124, 667.

Locke, G.B. (1953). J.Fac. Radiol., Lond., 5, 1.

Lombard, H.L., and Doering, C.R. (1928). New Engl. J. Med., 198, 481.

McAlpine, S.G. (1956). Brit. med. J., 2, 1412.

McCaughey, W.T.E., and Millar, J.M.D. (1955). Lancet, 2, 365.

McConnell, R.B., Clarke, C.A., and Downton, F. (1954). Brit. med. J., 2, 323.

———— Gordon, K.C.T., and Jones, T. (1952). Lancet, 2, 651.

McCort, J., and Robbins, L. (1951). Radiology, 57, 339.

MacHale, S.J. (1953). Thorax, 8, 164.

McKay, D., Ware, P., Atwood, D., and Harken, D. (1948). Cancer, 1, 208.

MacKay, N. (1957). Lancet, 2, 761.

McKenzie, A. (1956). Brit. med. J., 2, 204.

Mackle, W., and Gregorius, G. (1948). Pub. Hlth. Rep., 63, 1114.

Macklin, C.C. (1956). J. thorac. Surg., 31, 238.

Majumdar, N.K., and Zahn, D.W. (1957). Amer. Rev. Tuberc., 75, 644.

Marie, P. (1890). Rev. Médecine, 10, 1.

Mason, G.A. (1949). Lancet, 2, 587.

Mestitz, P., Pollard, A.C., and Purves, M.J. (1957). Lancet, 2, 873.

Middlemass, I.B.D. (1953). J.Fac. Radiol., Lond., 5, 121.

Miyaji, T., Kitamura, H., Senoo, T., Oda, T., and Murata, Y. (1955). Gann, 46, 523.

Moll, A. (1949). Med. Klinik, 44, 916.

Morrison, R. (1957). Personal communication.

———— and Deeley, T.J. (1957). Thorax, 12, 90.

Moyes, E.N. (1957). N.A.P.T. Bull., 20, 52.

Neuberger, F. (1956). Mschr. Ohrenheilk., 90, 373.

Nicholson, W.F., Fox, M., and Bryce, A.G. (1957). Lancet, 1, 296.

Nohl, H.C. (1956). Thorax, 11, 172.

Novak, J. (1956). Rozhl. Tuberk., 16, 40.

Nuessle, W.F. (1953). Dis. Chest, 23, 207.

Ochsner, A. (1952). Chocurua lung conference. Report of the American Cancer Society, Inc., 521 W.57th St., New York.

———— and Debakey, M. (1942). J. thorac. Surg. 11, 357.

Ochsner, A., Decamp, P., Debakey, M., and Rae, C. (1952). J. Amer. med. Ass., 148, 691.

———— Gibbon, J., and Jones, J.C. (1955). Arch. Surg., Chicago, 70, 265.

Oswald, N.C. (1956). Brit. med. J., 1, 711.

Overholt, R.H. (1950). Amer. Rev. Tuberc., 62, 491.

————and Bougas, J.A. (1956a). Dis. Chest, 29, 595.

———————— (1956b). J. thorac. Surg., 32, 508.

———————— and Woods, F.M. (1955). New Engl. J. Med., 252, 429.

———— and Schmidt, I.C. (1949). Ibid, 240, 491.

Pancoast, H.K. (1932). J.Amer. med. Ass., 99, 1391.

Pannett, C.A. (1957). Lancet, 1, 829.

Papanicolaou, G.N. (1956). N.Y. st. J. Med., 56, 2647.

———— and Cromwell, H.A.R. (1949). Dis. Chest, 15, 412.

———— and Liebow, A.A. (1956). in Pulmonary Carcinoma, New York University Press, New York.

Paracelsus, T. (1567). Von der Bergsucht. S. Mayer, Dilingen.

Pattison, J.D., Beck, E., and Miller, W.B. (1951). J. Amer. med. Ass., 146, 783.

Peterson, A.B., Hunter, W.C., and Sneeden, V.D. (1949). Cancer, 2,991.

Philps, E.R. (1954). Brit. J. Cancer, 8, 62.

Phillips, F.J., Basinger, C.E., and Adams, W.E. (1950). J. thorac. Surg., 19, 680.

Pirchan, A., and Sikl, H. (1932). Amer. J. Cancer, 16, 681.

Price Thomas, C. (1954). Lancet, 1, 1.

———— (1955). Practitioner, 174, 298.

———— and Drew, C.E. (1953). Thorax, 8, 180.

Putton, M.M., McDonald, J.R., and Moersch, H.J. (1951). J. thorac. Surg. 22, 83.

Raeburn, C. and Spencer, H. (1953). Thorax, 8, 1.

———————— ——— (1957). Brit. J. Tuberc., 51, 237.

Ray, E.S., and Fisher, M.P. (1953). Ann. Intern. Med., 38, 239.

Registrar General of England and Wales (1950 - 1956). Statistical Reviews. Part I. H.M.Stationery Office. London.

Registrar General of England and Wales (1954). Decennial Supplement 1951. Part I. H.M.Stationery Office. London.

Registrar General of England and Wales (1954). Statistical Review. Part III. H.M. Stationery Office. London.

Reid, D.D., and Buck, C. (1956). Brit. J. industr. Med., 13, 265.

Reports of Medical Officer of Health for Bedfordshire 1950 to 1956.

Rigdon, R.H., and Kirchoff, H. (1952). Tex. Rep. Biol. Med., 10, 76.

Rigler, L.G. (1952). Chocurua lung conference. Report of the American Cancer Society, Inc., 521 W. 57th St., New York.

———— and O'Loughlin, B.J., and Tucker, R.C. (1953). Dis. Chest, 23, 1.

Ringertz, N. (1955). Schweiz. Z. Path., 18, 866.

Robinson, C.L., and Peckar, V.G. (1956). Brit. J. Tuberc., 50, 205.

Rokitansky, C. van (1854). Manual of Pathological Anatomy. Sydenham Society, London.

Rosenblatt, M.B., and Lisa, J.R. (1957). Carcinoma of the Lung. Oxford University Press, New York.

Ross, W.M. (1957). Brit. med. J. 2, 708.

Roswit, B. (1955). Amer. J. Surg., 89, 538.

Sakula, A. (1955). Brit. med. J., 1, 759.

Scamman, C.L. (1951). New Engl. J. Med., 244, 541.

Schuster, N. (1955). Tubercle, Lond., 36, 350.

Schvarcz, J. (1955). Acta radiol., Stockh, 44, 89.

Seelkopf, C. (1955). 2. LebensmittUntersuch., 100, 218.

Sellors, T.H. (1955). Brit. med. J., 1, 445.

Semple, T., and McCluskie, R.A. (1955). Ibid, 1, 754.

Seyfarth, K.A. (1952). Acta daros. 11, 20.

Shanks, S.C., and Kerley, P. (1950). A Text-Book of X-ray Diagnosis, ed. II, H.K. Lewis, London.

Sherman, R.S. (1956). Pulmonary Carcinoma.

Sichel, D., Forster, E., Roegel, E., Mme Voegtlin, and Mlle Lenz, (1954). J. Radiol. Electrol., 35, 216.

Siegal, W., Plunkett, R.E., and Locke, B.Z. (1955). J. Amer. med. Ass., 157, 435.

Simpson, J.R. (1956). Harper Hosp. Bull., 14, 18.

Skinner, E.F., Hall, J., Carr, D., and Robbins, S.G. (1955). Amer. Surg., 21, 590.

Slessor, B.V., Britt, R.G., and Freer, J.L. (1954). Thorax, 9, 91.

Smart, J., and Hilton, G. (1956). Lancet, 1, 880.

Smiley, T.B., and Cheeseman, E.A. (1956). Ulster med. J., 25, 62.

Smith, R.A. (1954). Brit. J. Tuberc., 48, 311.

———— (1957). Thorax, 12, 79.

Smithers, D.W. (1953). Brit. med. J., 1, 1235.

———————— (1955). J. Fac. Radiol., Lond., 6, 174.

Spencer, H., and Raeburn, C. (1956). J. Path. Bact., 71, 145.

Spjut, H.J., Frier, D.J., and Ackerman, L.V. (1955). J. thorac. Surg., 30, 90.

Spriggs, A.I. (1954). Thorax, 9, 26.

Steinberg, I. and Robb, G.B. (1938). Amer. Rev. Tuberc., 38, 57.

Steiner, P.E. (1953). Acta Un. int. Cancr., 9, 450.

———————— Butt, E.M., and Edmondson, H.A. (1950). J. nat. Cancer Inst., 11, 497.

Stocks, P. (1953). Brit. J. Cancer, 7, 283.

———— (1954). Rep. Brit. Emp. Cancer Campaign 32nd. Ann. Rep., 485.

———— and Campbell, J.M. (1955). Brit. med. J. 2, 923.

Storey, C.F., Knudtson, K.P., and Lawrence, B.J. (1953). J. thorac. Surg., 26, 331.

Strang, C., and Simpson, J.A. (1953). Thorax, 8, 11.

Szur, L. (1957). Personal communication.

Szur and Bromley, L.L. (1956). Brit. med. J., 11, 1273.

Tanner, G.R., and Gordon, H. (1952). Amer. J. Path., 28, 953.

Taylor, A.B., and Waterhouse, J.A.H. (1950). Thorax, 5, 257.

Thompson, V.C. (1957). N.A.P.T. Bull., 20, 2.

Toft, G. (1955). Acta path. microbiol. scand., 105, 219.

Tripoli, C.J., and Holland, L.F. (1940). Sth. med. J., 33, 559.

Trousseau, A. (1877). Clinique Médicale de l'Hôtel Dieu de Paris. 5th ed. Baileière, Paris.

Umiker, W. (1956). Transactions of the 15th U.S. Conference on the Chaemotherapy of Tuberculosis. Dept. of Medicine and Surgery, Central Office, Washington.

Van Hazel, W, (1939). J. thorac. Surg., 9, 495.

Victor, A.B. (1955). Dis. Chest, 27, 4.

Vogl, A., Blumenfeld, S., and Gutner, L.B. (1953). Amer. J. Med., 18, 51.

Waller, R.E. (1952). Brit. J. Cancer, 6, 8.

Walter, J.B., and Price, D.M. (1955a). Thorax, 10, 107.

———————————— (1955b). Ibid, 10, 117.

Wandall, H. (1944). Acta chir. scand., Supp. 93, 91, 1.

Wanscher, O., Clemmesen, J., and Nielson, A. (1951). Brit. J. Cancer, 5, 172.

Warfvinge, L.E. (1956). Acta med. scand. 153, 49.

Watson, T.A.(1956). Amer. J. Roentgenol., 75, 525.

Watson, W., Cromwell, H., Craver, L.R., and Papanicolaou, G. (1949). J. thorac. Surg., 18, 113.

Williams, A.A. (1954). Brit. med. J., 2, 82.

Willis, R.A. (1953). Pathology of Tumors. 2nd ed., Butterworth, London.

Winternitz, M.C., Wason, I.M., and McNamara, F.R. (1920). The Pathology of Influenza. Yale University Press, New Haven.

Wood, D.A., and Miller, M. (1938). J. thorac. Surg., 7, 649.

Woodruff, C.E., and Nahas, H.C. (1951). Amer. Rev. Tuberc., 64, 620.

Woolner, L., and McDonald, J. (1949). Amer. J. clin. Path., 19, 765.

Wynder, E.L., and Graham, E.A. (1950). J. Amer. med. Ass., 143, 329.

Young, R.D. (1954). Brit. med. J., 2, 631.

Zaman, H. (1955). Brit. J. tuberc., 49, 266.

Zeil, R. (1935). Med. Klinik, 31, 1535.

Zheutlin, N., Lasser, E.C., and Rigler, L.G. (1954). Dis. Chest, 25, 542.

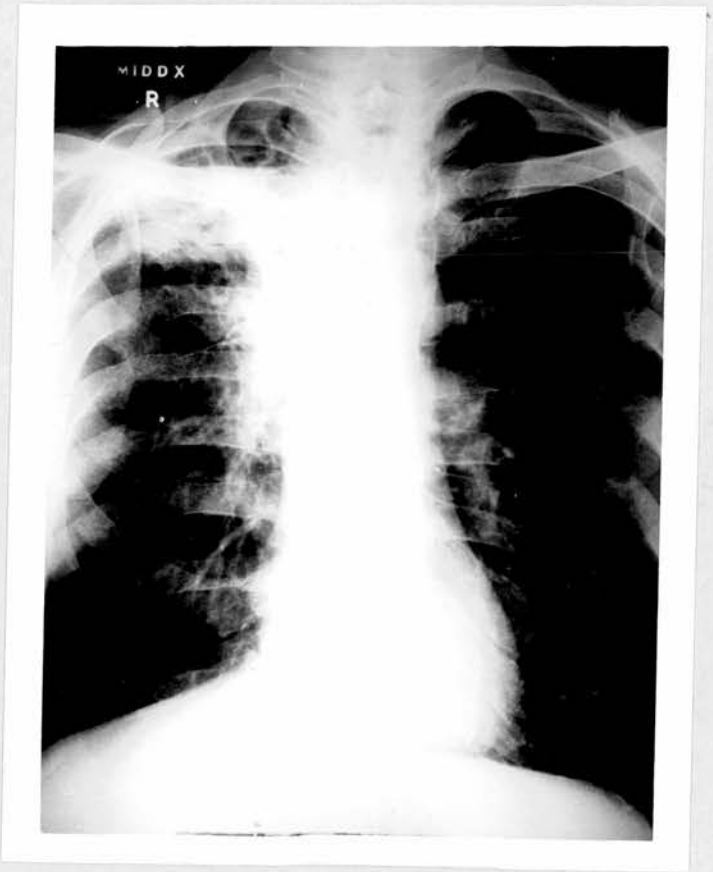
Zizmor, J.(1955). Radiology, 65, 868.

APPENDIX

RADIOGRAPHIC REPRODUCTIONS

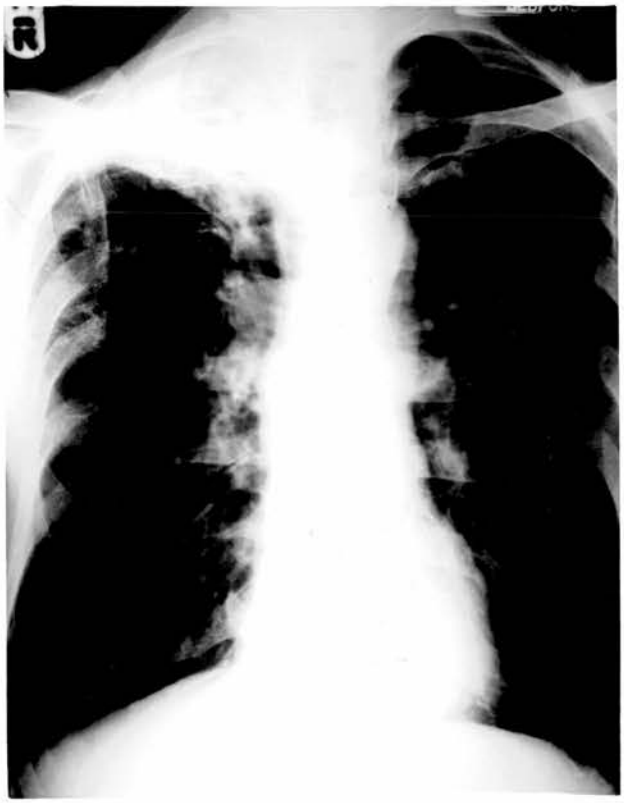
PLATES 1-36

PLATE 1



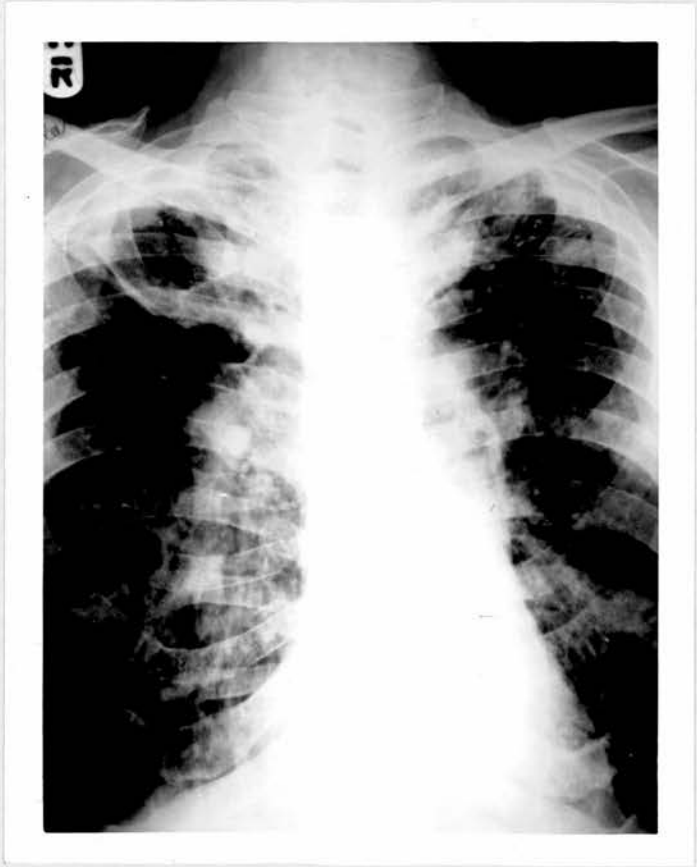
Case 18996. P.A. radiograph, 11.7.45, showing diffuse shadow in the right upper zone.

PLATE 2



Same case as Plate I. P.A. radiograph, 5.11.53, showing superior sulcus tumour. The full syndrome was present, rib erosion shown on tomography, Plate 34.

PLATE 3

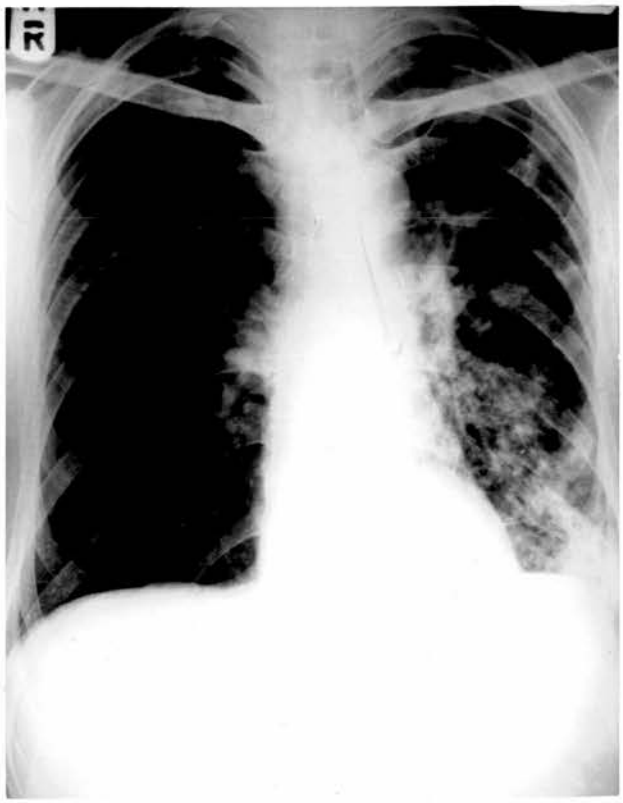


Case 21127. P.A. radiograph, 24.3.55, showing extensive pulmonary tuberculosis with cavitation.

PLATE 4

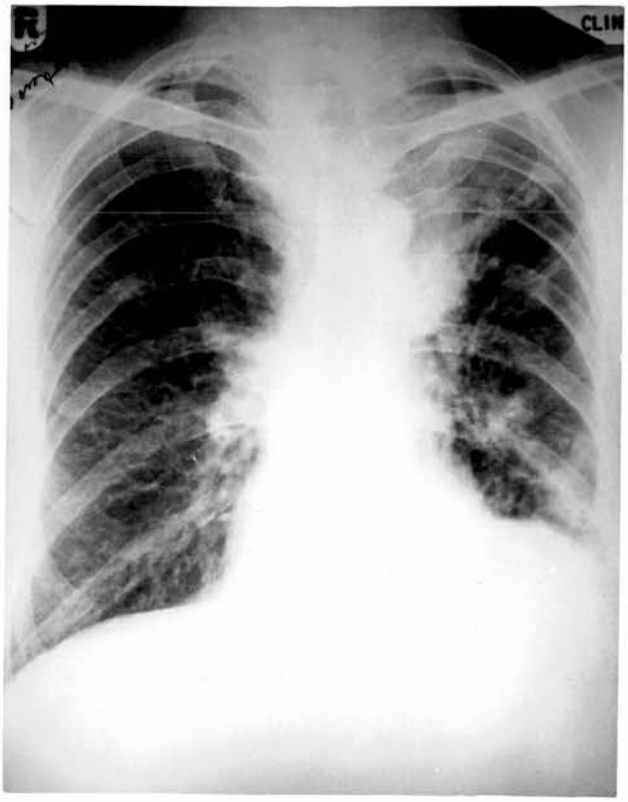
Same case as Plate 3. P.A. radiograph, 9.12.55, showing development of carcinoma in left upper zone. Superior sulcus syndrome present.

PLATE 5



Case 23324. P.A. radiograph, 10.5.56, showing extensive pulmonary tuberculosis throughout the left lung, to a lesser extent in the right lung.

PLATE 6



Same case as Plate 5. P.A. radiograph, 7.2.57, showing (a) partial resolution of tuberculosis, (b) development of carcinoma in left middle and upper zones, (c) elevation of left diaphragm due to phrenic paralysis.

PLATE 7

Case 20097. P.A radiograph showing shadow of carcinoma behind anterior end of first left rib. The patient had no pulmonary symptoms and was picked up by miniature (70 mm) radiography when attending an ante-natal clinic.

PLATE 8

Case 16921. P.A. radiograph showing enlargement of the left hilar shadow. The patient had no pulmonary symptoms at this time.

PLATE 9

Case 20013. P.A. radiograph showing consolidation due to carcinoma in the right lower lobe.

PLATE 10

Case 19685. P.A. radiograph showing collapse/consolidation in the middle lobe.

PLATE 11

Same case as Plate 10. Right lateral radiograph confirming P.A. view.

PLATE 12

Case 22972. P.A. radiograph showing (a) collapse/ consolidation in the right upper lobe with predominence of collapse, and (b) enlargement of hilar shadow.

PLATE 13

Same case as Plate 12. Right lateral radiograph confirming P.A. view.

PLATE 14

Case 13866. P.A. radiograph showing a peripheral mass in the right upper lobe, without any hilar enlargement.

PLATE 15

Case 17313. P.A. radiograph showing (a) diffuse shadowing in the right lower lobe, and (b) enlargement of hilar shadow.

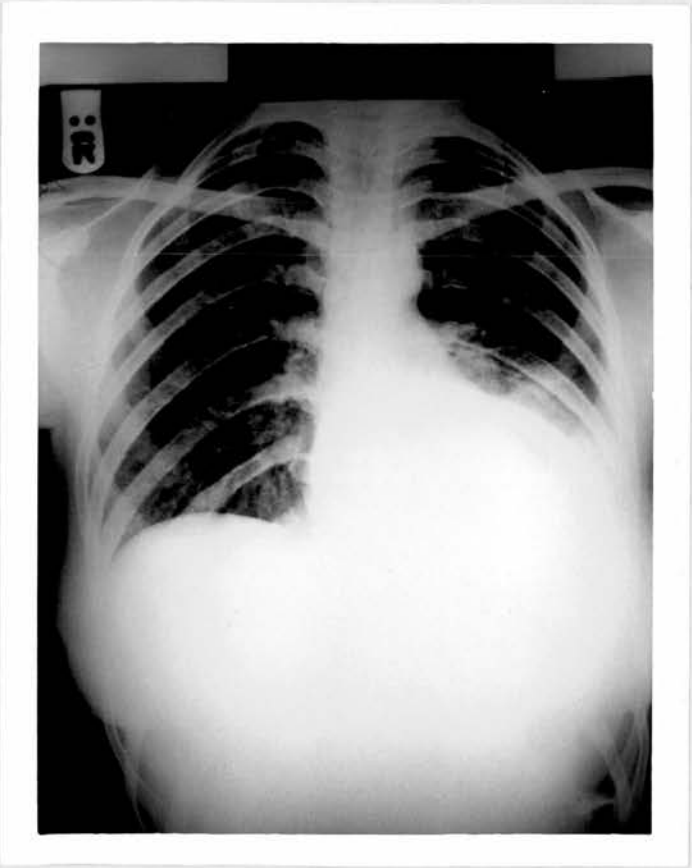
PLATE 16

Case 24076. P.A. radiograph showing only enlargement of the right hilar shadow. The growth was situated in the right main bronchus.

PLATE 17

Same case as Plate 16. Right lateral radiograph showing enlargement of the right hilar shadow anterior to the lower end of the trachea.

PLATE 18



Case 21227. P.A. radiograph showing left pleural effusion. The growth was situated in the left lower lobe.

PLATE 19

Case 9574. P.A. radiograph showing (a) left pleural effusion, and (b) diffuse shadowing in the left upper zone.

PLATE 20

Case 14629. P.A. radiograph showing (a) a large malignant abscess in the right middle and lower zones, and (b) elevation of the right diaphragm due to phrenic paralysis. The growth was situated in the right main bronchus.

PLATE 21

Case 10764. P.A. radiograph showing massive collapse of the right lung. The growth was situated in the right main bronchus.

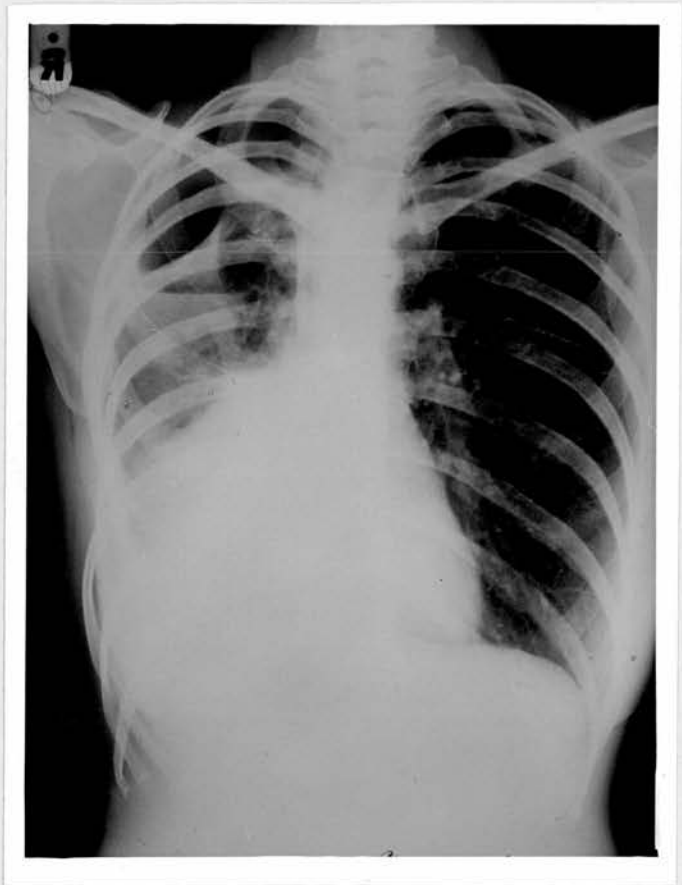
PLATE 22

Case 11571. P.A. radiograph showing only a broadened mediastinum. The growth was situated in the left main bronchus.

PLATE 23

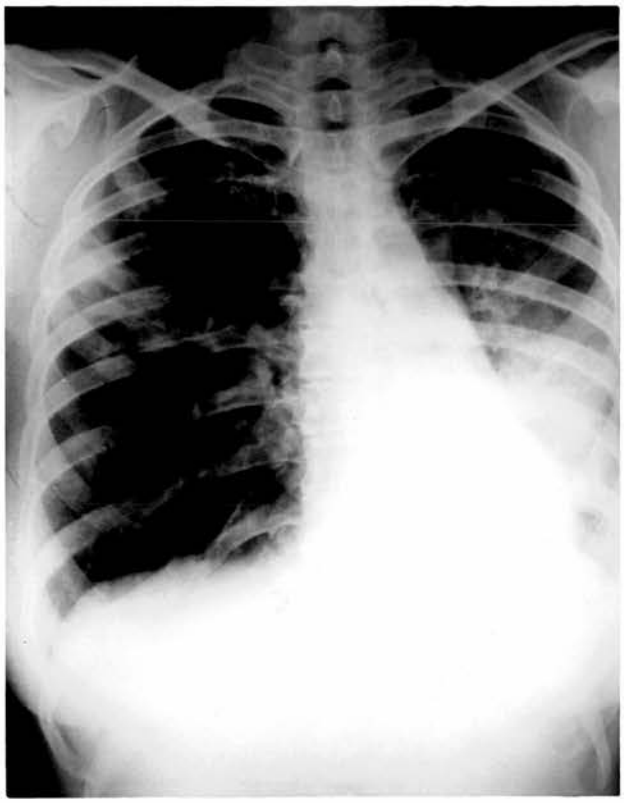
Case 7077. P.A. radiograph showing (a) tumour mass in the left middle and upper zones due to a left upper lobe growth, and (b) secondary deposits in the left middle zone and at the lower pole if the right hilum.

PLATE 24



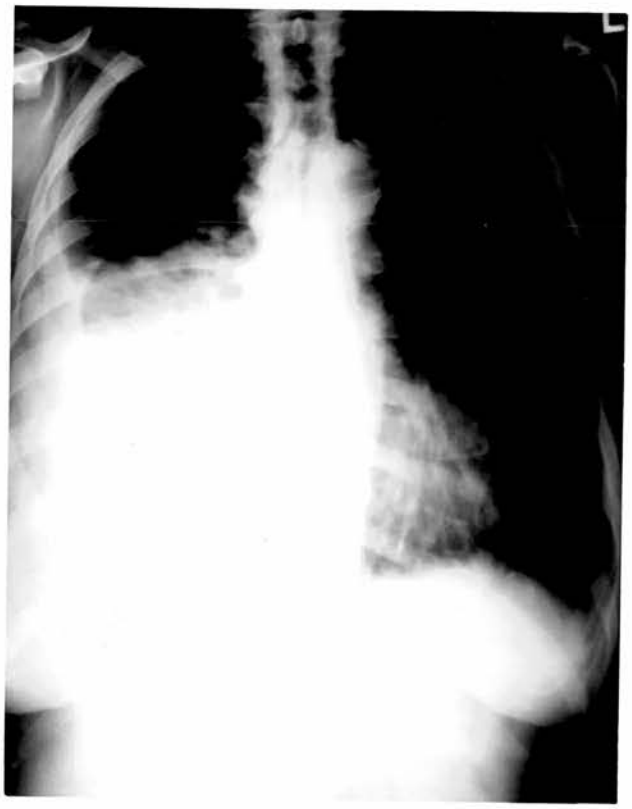
Case 10779. P.A. radiograph showing (a) a pneumothorax, containing a fluid level, in the right upper zone, and (b) collapse consolidation of the right lower lobe.

PLATE 25



Case 10204. P.A. radiograph, showing (a) collapse/ consolidation in the left middle and lower zones, associated with some mediastinal displacement, and (b) diffuse shadowing in the right middle zone. Bronchiolar carcinoma.

PLATE 26

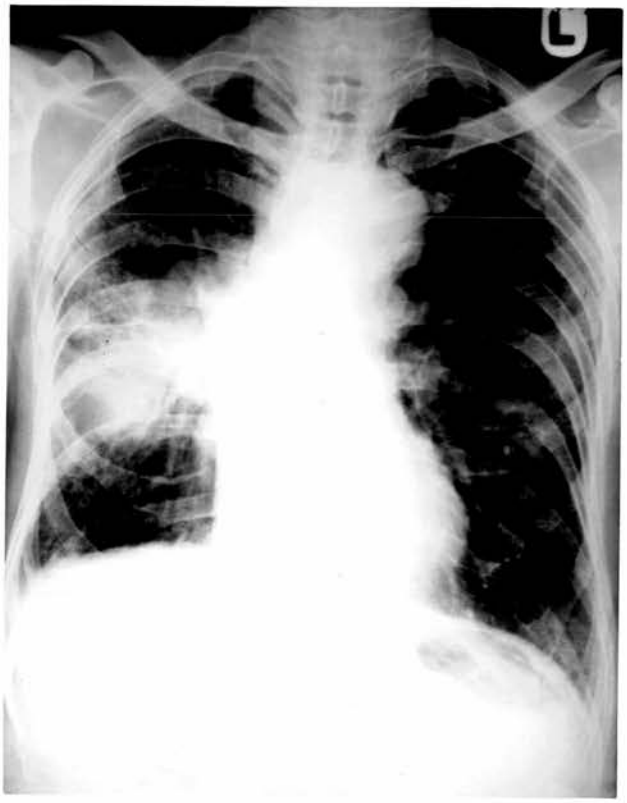


Case 12494. P.A. radiograph (penetrated), showing (a) a right pleural effusion, and (b) diffuse shadowing underlying it. Bronchiolar carcinoma.

PLATE 27

Same case as Plate 26. Right lateral radiograph, showing diffuse shadowing in the middle and lower lobes.

PLATE 28



Case 14921. P.A. radiograph showing a diffuse opacity in the right middle zone. Bronchilar carcinoma.

PLATE 29

Case 23927. P.A. radiograph showing widespread mottling throughout the lung fields. Fragments of a metallic foreign body are present in the periphery of the right upper and middle zones. Bronchiolar carcinoma.

PLATE 30

Case 13866. A.P. tomograph showing unsuspected central cavitation in a tumour mass situated in the right upper zone.

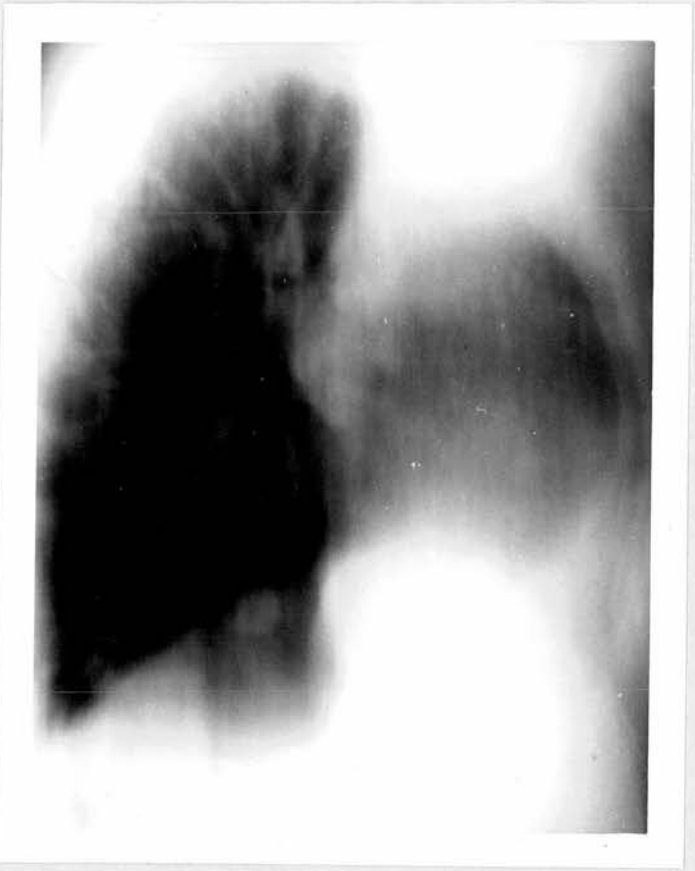
PLATE 31

Case 20346. P.A. radiograph showing consolidation in left upper lobe.

PLATE 32

Same case as Plate 31. A.P. tomograph showing in addition to the primary shadow, a secondary deposit close to the mediastinum in the right lower lobe.

PLATE 33



Same case as Plate 31. Right lateral tomograph showing the secondary deposit in right lower lobe.

PLATE 34

Case 18996. A.P. tomograph showing erosion of third right rib. Superior sulcus tumour. Same case as Plates 1 and 2.

PLATE 35

Case 20429. Bronchogram right lung, right posterior oblique view showing complete tapering stenosis of right stem bronchus just below the origin of the upper lobe bronchus. The upper lobe fills the hemithorax.

PLATE 36

Case 23945. Bronchogram, left lung, left posterior oblique view showing complete transverse stenosis of the posterior branch of the apico-posterior bronchus of the left upper lobe.

PLATE 37

Case 17324. P.A. radiograph, 5.9.50, showing triangular shadow projecting from left hilum.

PLATE 38

Same case as Plate 37. P.A. radiograph, 13.10.55, showing considerable extension of shadowing throughout the whole of the left hemithorax.